JC828 U.S. PTO
09/933767
08/22/01

PD-P2980 "09/933767

207 Human Secreted Proteins

This application is a continuation-in-part of, and claims benefit under 35 U.S.C. § 120 of copending International patent application Serial No: PCT/US01/05614 (in English), filed February 21, 2001, which is hereby incorporated by reference, which claims benefit under 35 U.S.C. § 119(e) based on U.S. Provisional Patent Application Serial Nos. 60/184,836 filed February 24, 2000 and 60/193,170 filed March 29, 2000, both of which are hereby incorporated by reference, and this application is a continuation-in-part of, and claims benefit under 35 U.S.C. § 120 of copending United States patent application Serial No. 09/205,258 filed December 4, 1998, which is hereby incorporated by reference, and which claims benefit under 35 U.S.C. § 120 of International patent application No.: PCT/US98/11422 (in English), filed June 4, 1998, which is hereby incorporated by reference, which claims benefit under 35 U.S.C. § 119(e) based on U.S. Provisional Applications, all of which are hereby incorporated by reference:

	Filing Date	Appln No.
1.	06-Jun-1997	60/048,885
2.	06-Jun-1997	60/049,375
3.	06-Jun-1997	60/048,881
4.	06-Jun-1997	60/048,880
5.	06-Jun-1997	60/048,896
6.	06-Jun-1997	60/049,020
7.	06-Jun-1997	60/048,876
8.	06-Jun-1997	60/048,895
9.	06-Jun-1997	60/048,884
10.	06-Jun-1997	60/048,894
11.	06-Jun-1997	60/048,971
12.	06-Jun-1997	60/048,964
13.	06-Jun-1997	60/048,882
14.	06-Jun-1997	60/048,899
15.	06-Jun-1997	60/048,893
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20.	06-Jun-1997	60/049,019
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22.	06-Jun-1997	60/048,972
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73.	18-Dec-1997	60/070,923

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74.	15-Jul-1998	60/092,921
75.	30-Jul-1998	60/094,657
76.	18-Dec-1997	60/070,923
77.	15-Jul-1998	60/092,921
78.	30-Jul-1998	60/094,657

Field of the Invention

This invention relates to newly identified polynucleotides, polypeptides encoded by these polynucleotides, antibodies that bind these polypeptides, uses of such polynucleotides, polypeptides, and antibodies, and their production.

Background of the Invention

Unlike bacterium, which exist as a single compartment surrounded by a membrane, human cells and other eucaryotes are subdivided by membranes into many functionally distinct compartments. Each membrane-bounded compartment, or organelle, contains different proteins essential for the function of the organelle. The cell uses "sorting signals," which are amino acid motifs located within the protein, to target proteins to particular cellular organelles.

One type of sorting signal, called a signal sequence, a signal peptide, or a leader sequence, directs a class of proteins to an organelle called the endoplasmic reticulum (ER). The ER separates the membrane-bounded proteins from all other types of proteins. Once localized to the ER, both groups of proteins can be further directed to another organelle called the Golgi apparatus. Here, the Golgi distributes the proteins to vesicles, including secretory vesicles, the cell membrane, lysosomes, and the other organelles.

Proteins targeted to the ER by a signal sequence can be released into the extracellular space as a secreted protein. For example, vesicles containing secreted proteins can fuse with the cell membrane and release their contents into the extracellular space - a process called exocytosis. Exocytosis can occur constitutively or after receipt of a triggering signal. In the latter case, the proteins are stored in secretory vesicles (or secretory granules) until exocytosis is triggered. Similarly, proteins residing on the cell membrane can also be secreted into the extracellular space by proteolytic cleavage of a "linker" holding the protein to the membrane.

Despite the great progress made in recent years, only a small number of genes encoding human secreted proteins have been identified. These secreted proteins include the commercially valuable human insulin, interferon, Factor VIII, human growth hormone, tissue plasminogen activator, and erythropoeitin. Thus, in light of the pervasive role of secreted proteins in human physiology, a need exists for identifying and characterizing novel human secreted proteins and the genes that encode them. This knowledge will allow one to detect, to treat, and to prevent medical diseases, disorders, and/or conditions by using secreted proteins or the genes that encode them.

Summary of the Invention

The present invention relates to novel polynucleotides and the encoded polypeptides. Moreover, the present invention relates to vectors, host cells, antibodies, and recombinant and synthetic methods for producing the polypeptides and polynucleotides. Also provided are diagnostic methods for detecting diseases, disorders, and/or conditions related to the polypeptides and polynucleotides, and therapeutic methods for treating such diseases, disorders, and/or conditions. The invention further relates to screening methods for identifying binding partners of the polypeptides.

Detailed Description

Definitions

The following definitions are provided to facilitate understanding of certain terms used throughout this specification.

In the present invention, "isolated" refers to material removed from its original environment (e.g., the natural environment if it is naturally occurring), and thus is altered "by the hand of man" from its natural state. For example, an isolated polynucleotide could be part of a vector or a composition of matter, or could be contained within a cell, and still be "isolated" because that vector, composition of matter, or particular cell is not the original environment of the polynucleotide. The term "isolated" does not refer to genomic or cDNA libraries, whole cell total or mRNA preparations, genomic DNA preparations (including those separated by electrophoresis and transferred onto blots), sheared whole cell genomic DNA

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preparations or other compositions where the art demonstrates no distinguishing features of the polynucleotide/sequences of the present invention.

In the present invention, a "secreted" protein refers to those proteins capable of being directed to the ER, secretory vesicles, or the extracellular space as a result of a signal sequence, as well as those proteins released into the extracellular space without necessarily containing a signal sequence. If the secreted protein is released into the extracellular space, the secreted protein can undergo extracellular processing to produce a "mature" protein. Release into the extracellular space can occur by many mechanisms, including exocytosis and proteolytic cleavage.

In specific embodiments, the polynucleotides of the invention are at least 15, at least 30, at least 50, at least 100, at least 125, at least 500, or at least 1000 continuous nucleotides but are less than or equal to 300 kb, 200 kb, 100 kb, 50 kb, 15 kb, 10 kb, 7.5 kb, 5 kb, 2.5 kb, 2.0 kb, or 1 kb, in length. In a further embodiment, polynucleotides of the invention comprise a portion of the coding sequences, as disclosed herein, but do not comprise all or a portion of any intron. In another embodiment, the polynucleotides comprising coding sequences do not contain coding sequences of a genomic flanking gene (i.e., 5' or 3' to the gene of interest in the genome). In other embodiments, the polynucleotides of the invention do not contain the coding sequence of more than 1000, 500, 250, 100, 50, 25, 20, 15, 10, 5, 4, 3, 2, or 1 genomic flanking gene(s).

As used herein, a "polynucleotide" refers to a molecule having a nucleic acid sequence contained in SEQ ID NO:X or the cDNA contained within the clone deposited with the ATCC. For example, the polynucleotide can contain the nucleotide sequence of the full length cDNA sequence, including the 5' and 3' untranslated sequences, the coding region, with or without the signal sequence, the secreted protein coding region, as well as fragments, epitopes, domains, and variants of the nucleic acid sequence. Moreover, as used herein, a "polypeptide" refers to a molecule having the translated amino acid sequence generated from the polynucleotide as broadly defined.

In the present invention, the full length sequence identified as SEQ ID NO:X was often generated by overlapping sequences contained in multiple clones (contig analysis). A representative clone containing all or most of the sequence for SEQ ID

NO:X was deposited with the American Type Culture Collection ("ATCC"). As shown in Table 1, each clone is identified by a cDNA Clone ID (Identifier) and the ATCC Deposit Number. The ATCC is located at 10801 University Boulevard, Manassas, Virginia 20110-2209, USA. The ATCC deposit was made pursuant to the terms of the Budapest Treaty on the international recognition of the deposit of microorganisms for purposes of patent procedure.

A "polynucleotide" of the present invention also includes those polynucleotides capable of hybridizing, under stringent hybridization conditions, to sequences contained in SEQ ID NO:X, the complement thereof, or the cDNA within the clone deposited with the ATCC. "Stringent hybridization conditions" refers to an overnight incubation at 42 degree C in a solution comprising 50% formamide, 5x SSC (750 mM NaCl, 75 mM trisodium citrate), 50 mM sodium phosphate (pH 7.6), 5x Denhardt's solution, 10% dextran sulfate, and 20 μg/ml denatured, sheared salmon sperm DNA, followed by washing the filters in 0.1x SSC at about 65 degree C.

Also contemplated are nucleic acid molecules that hybridize to the polynucleotides of the present invention at lower stringency hybridization conditions. Changes in the stringency of hybridization and signal detection are primarily accomplished through the manipulation of formamide concentration (lower percentages of formamide result in lowered stringency); salt conditions, or temperature. For example, lower stringency conditions include an overnight incubation at 37 degree C in a solution comprising 6X SSPE (20X SSPE = 3M NaCl; 0.2M NaH_2PO_4; 0.02M EDTA, pH 7.4), 0.5% SDS, 30% formamide, 100 ug/ml salmon sperm blocking DNA; followed by washes at 50 degree C with 1XSSPE, 0.1% SDS. In addition, to achieve even lower stringency, washes performed following stringent hybridization can be done at higher salt concentrations (e.g. 5X SSC).

Note that variations in the above conditions may be accomplished through the inclusion and/or substitution of alternate blocking reagents used to suppress background in hybridization experiments. Typical blocking reagents include Denhardt's reagent, BLOTTO, heparin, denatured salmon sperm DNA, and commercially available proprietary formulations. The inclusion of specific blocking

reagents may require modification of the hybridization conditions described above, due to problems with compatibility.

Of course, a polynucleotide which hybridizes only to polyA+ sequences (such as any 3' terminal polyA+ tract of a cDNA shown in the sequence listing), or to a complementary stretch of T (or U) residues, would not be included in the definition of "polynucleotide," since such a polynucleotide would hybridize to any nucleic acid molecule containing a poly (A) stretch or the complement thereof (e.g., practically any double-stranded cDNA clone generated using oligo dT as a primer).

The polynucleotide of the present invention can be composed of any polyribonucleotide or polydeoxribonucleotide, which may be unmodified RNA or DNA or modified RNA or DNA. For example, polynucleotides can be composed of single- and double-stranded DNA, DNA that is a mixture of single- and double-stranded regions, single- and double-stranded RNA, and RNA that is mixture of single- and double-stranded regions, hybrid molecules comprising DNA and RNA that may be single-stranded or, more typically, double-stranded or a mixture of single- and double-stranded regions. In addition, the polynucleotide can be composed of triple-stranded regions comprising RNA or DNA or both RNA and DNA. A polynucleotide may also contain one or more modified bases or DNA or RNA backbones modified for stability or for other reasons. "Modified" bases include, for example, tritylated bases and unusual bases such as inosine. A variety of modifications can be made to DNA and RNA; thus, "polynucleotide" embraces chemically, enzymatically, or metabolically modified forms.

The polypeptide of the present invention can be composed of amino acids joined to each other by peptide bonds or modified peptide bonds, i.e., peptide isosteres, and may contain amino acids other than the 20 gene-encoded amino acids. The polypeptides may be modified by either natural processes, such as posttranslational processing, or by chemical modification techniques which are well known in the art. Such modifications are well described in basic texts and in more detailed monographs, as well as in a voluminous research literature. Modifications can occur anywhere in a polypeptide, including the peptide backbone, the amino acid side-chains and the amino or carboxyl termini. It will be appreciated that the same type of modification may be present in the same or varying degrees at several sites in

a given polypeptide. Also, a given polypeptide may contain many types of modifications. Polypeptides may be branched , for example, as a result of ubiquitination, and they may be cyclic, with or without branching. Cyclic, branched, and branched cyclic polypeptides may result from posttranslation natural processes or may be made by synthetic methods. Modifications include acetylation, acylation, ADP-ribosylation, amidation, covalent attachment of flavin, covalent attachment of a heme moiety, covalent attachment of a nucleotide or nucleotide derivative, covalent attachment of a lipid or lipid derivative, covalent attachment of phosphotidylinositol, cross-linking, cyclization, disulfide bond formation, demethylation, formation of covalent cross-links, formation of cysteine, formation of pyroglutamate, formylation, gamma-carboxylation, glycosylation, GPI anchor formation, hydroxylation, iodination, methylation, myristoylation, oxidation, pegylation, proteolytic processing, phosphorylation, prenylation, racemization, selenoylation, sulfation, transfer-RNA mediated addition of amino acids to proteins such as arginylation, and ubiquitination. (See, for instance, PROTEINS - STRUCTURE AND MOLECULAR PROPERTIES, 2nd Ed., T. E. Creighton, W. H. Freeman and Company, New York (1993); POSTTRANSLATIONAL COVALENT MODIFICATION OF PROTEINS, B. C. Johnson, Ed., Academic Press, New York, pgs. 1-12 (1983); Seifter et al., Meth Enzymol 182:626-646 (1990); Rattan et al., Ann NY Acad Sci 663:48-62 (1992).)

"SEQ ID NO:X" refers to a polynucleotide sequence while "SEQ ID NO:Y" refers to a polypeptide sequence, both sequences identified by an integer specified in Table 1.

"A polypeptide having biological activity" refers to polypeptides exhibiting activity similar, but not necessarily identical to, an activity of a polypeptide of the present invention, including mature forms, as measured in a particular biological assay, with or without dose dependency. In the case where dose dependency does exist, it need not be identical to that of the polypeptide, but rather substantially similar to the dose-dependence in a given activity as compared to the polypeptide of the present invention (i.e., the candidate polypeptide will exhibit greater activity or not more than about 25-fold less and, preferably, not more than about tenfold less activity, and most preferably, not more than about three-fold less activity relative to the polypeptide of the present invention.)

Polynucleotides and Polypeptides of the Invention

FEATURES OF PROTEIN ENCODED BY GENE NO: 1

This gene is expressed primarily in melanocytes and, to a lesser extent, in testes, ovary, kidney and other tissues.

Polynucleotides and polypeptides of the invention are useful as reagents for differential identification of the tissue(s) or cell type(s) present in a biological sample and for diagnosis of diseases and conditions which include, but are not limited to, disorders of neural crest derived cells including pigmentation defects, melanoma, reproductive organ defects, and defects of the kidney . Similarly, polypeptides and antibodies directed to these polypeptides are useful in providing immunological probes for differential identification of the tissue(s) or cell type(s). For a number of disorders of the above tissues or cells, particularly of the skin, reproductive, and renal systems, expression of this gene at significantly higher or lower levels may be routinely detected in certain tissues or cell types (e.g. melanocytes, testes, ovary, kidney, cancerous and wounded tissues) or bodily fluids (e.g., lymph, serum, plasma, urine, synovial fluid and spinal fluid) or another tissue or cell sample taken from an individual having such a disorder, relative to the standard gene expression level, i.e., the expression level in healthy tissue or bodily fluid from an individual not having the disorder.

The tissue distribution in melanocytes indicates that the protein product of this gene is useful for treating disorders that arise from alterations in the number or fate of neural crest derived cells including cancers such as melanoma and defects of the developing reproductive system.

Many polynucleotide sequences, such as EST sequences, are publicly available and accessible through sequence databases. Some of these sequences are related to SEQ ID NO:11 and may have been publicly available prior to conception of the present invention. Preferably, such related polynucleotides are specifically excluded from the scope of the present invention. To list every related sequence is cumbersome. Accordingly, preferably excluded from the present invention are one or more polynucleotides comprising a nucleotide sequence described by the general formula of a-b, where a is any integer between 1 to 2512 of SEQ ID NO:11, b is an

integer of 15 to 2526, where both a and b correspond to the positions of nucleotide residues shown in SEQ ID NO:11, and where b is greater than or equal to a + 14.

FEATURES OF PROTEIN ENCODED BY GENE NO: 2

In specific embodiments, polypeptides of the invention comprise, or alternatively consists of, the following amino acid sequence: ENMICVKCLPQYPEHSKHV (SEQ ID NO:487). Moreover, fragments and variants of this polypeptide (such as, for example, fragments as described herein, polypeptides at least 80%, 85%, 90%, 95%, 96%, 97%, 98%, or 99% identical to these polypeptides and polypeptides encoded by the polynucleotide which hybridize, under stringent conditions, to the polynucleotide encoding this polypeptide are encompassed by the invention. Antibodies that bind polypeptides of the invention are also encompassed by the invention. Polynucleotides encoding this polypeptide are also encompassed by the invention.

This gene is expressed primarily in infant brain and fetal lung.

Polynucleotides and polypeptides of the invention are useful as reagents for differential identification of the tissue(s) or cell type(s) present in a biological sample and for diagnosis of diseases and conditions which include, but are not limited to, developmental disorders of the brain or lung. Similarly, polypeptides and antibodies directed to these polypeptides are useful in providing immunological probes for differential identification of the tissue(s) or cell type(s). For a number of disorders of the above tissues or cells, particularly of the central nervous and pulmonary systems, expression of this gene at significantly higher or lower levels may be routinely detected in certain tissues or cell types (e.g. brain, lung, cancerous and wounded tissues) or bodily fluids (e.g., lymph, serum, plasma, urine, synovial fluid and spinal fluid) or another tissue or cell sample taken from an individual having such a disorder, relative to the standard gene expression level, i.e., the expression level in healthy tissue or bodily fluid from an individual not having the disorder.

The tissue distribution in infant brain and fetal lung indicates that the protein product of this gene is useful for treating or diagnosing disorders associated with

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abnormal proliferation of cells in the Central nervous system and developing lung. Furthermore, the protein product of this gene is useful for the detection/treatment of neurodegenerative disease states and behavioral disorders such as Alzheimer's Disease, Parkinson's Disease, Huntington's Disease, Tourette's Syndrome, schizophrenia, mania, dementia, paranoia, obsessive compulsive disorder, panic disorder, learning disabilities, ALS, psychoses , autism, and altered behaviors, including disorders in feeding, sleep patterns, balance, and perception. In addition, the gene or gene product may also play a role in the treatment and/or detection of developmental disorders associated with the developing embryo, or sexually-linked disorders. Protein, as well as, antibodies directed against the protein may show utility as a tumor marker and/or immunotherapy targets for the above listed tissues.

Many polynucleotide sequences, such as EST sequences, are publicly available and accessible through sequence databases. Some of these sequences are related to SEQ ID NO:12 and may have been publicly available prior to conception of the present invention. Preferably, such related polynucleotides are specifically excluded from the scope of the present invention. To list every related sequence is cumbersome. Accordingly, preferably excluded from the present invention are one or more polynucleotides comprising a nucleotide sequence described by the general formula of a-b, where a is any integer between 1 to 1117 of SEQ ID NO:12, b is an integer of 15 to 1131, where both a and b correspond to the positions of nucleotide residues shown in SEQ ID NO:12, and where b is greater than or equal to a + 14.

FEATURES OF PROTEIN ENCODED BY GENE NO: 3

In specific embodiments, polypeptides of the invention comprise, or alternatively consists of, the following amino acid sequence: ARVAFHLICRYILPTVYCHV (SEQ ID NO:488). Moreover, fragments and variants of this polypeptide (such as, for example, fragments as described herein, polypeptides at least 80%, 85%, 90%, 95%, 96%, 97%, 98%, or 99% identical to these polypeptides and polypeptides encoded by the polynucleotide which hybridize, under stringent conditions, to the polynucleotide encoding this polypeptide are

encompassed by the invention. Antibodies that bind polypeptides of the invention are also encompassed by the invention. Polynucleotides encoding this polypeptide are also encompassed by the invention.

This gene is expressed primarily in breast lymph node, and to a lesser extent, in ovarian cancer and chondrosarcoma.

Polynucleotides and polypeptides of the invention are useful as reagents for differential identification of the tissue(s) or cell type(s) present in a biological sample and for diagnosis of diseases and conditions which include, but are not limited to, immune responses such as inflammation or immune surveillance for tumors. This gene may be important for inflammatory responses associated with tumors. Similarly, polypeptides and antibodies directed to these polypeptides are useful in providing immunological probes for differential identification of the tissue(s) or cell type(s). For a number of disorders of the above tissues or cells, particularly of the immune system, expression of this gene at significantly higher or lower levels may be routinely detected in certain tissues or cell types (e.g. lymph nodes, cancerous and wounded tissues) or bodily fluids (e.g. lymph, serum, plasma, urine, synovial fluid and spinal fluid) or another tissue or cell sample taken from an individual having such a disorder, relative to the standard gene expression level, i.e., the expression level in healthy tissue or bodily fluid from an individual not having the disorder.

Predicted epitopes include those comprising a sequence shown in SEQ ID NO: 251 as residues: Lys-45 to Val-50, and/or Lys-69 to Arg-76.

The tissue distribution in breast lymph node indicates that the protein product of this gene is useful for the treatment or diagnosis of immune responses, including those associated with tumor-induced inflammation. Furthermore, given the tissue distribution, the gene product may also be involved in lymphopoiesis. In a case such as this, it can be used in immune disorders such as infection, inflammation, allergy, immunodeficiency etc. Protein, as well as, antibodies directed against the protein may show utility as a tumor marker and/or immunotherapy targets for the above listed tissues.

Many polynucleotide sequences, such as EST sequences, are publicly available and accessible through sequence databases. Some of these sequences are related to SEQ ID NO:13 and may have been publicly available prior to conception of

the present invention. Preferably, such related polynucleotides are specifically excluded from the scope of the present invention. To list every related sequence is cumbersome. Accordingly, preferably excluded from the present invention are one or more polynucleotides comprising a nucleotide sequence described by the general formula of a-b, where a is any integer between 1 to 927 of SEQ ID NO:13, b is an integer of 15 to 941, where both a and b correspond to the positions of nucleotide residues shown in SEQ ID NO:13, and where b is greater than or equal to a + 14.

FEATURES OF PROTEIN ENCODED BY GENE NO: 4

In specific embodiments, polypeptides of the invention comprise, or alternatively consists of, the following amino acid sequence: ELVESPGAAGNSARSGNVVC (SEQ ID NO:489). Moreover, fragments and variants of this polypeptide (such as, for example, fragments as described herein, polypeptides at least 80%, 85%, 90%, 95%, 96%, 97%, 98%, or 99% identical to these polypeptides and polypeptides encoded by the polynucleotide which hybridize, under stringent conditions, to the polynucleotide encoding this polypeptide are encompassed by the invention. Antibodies that bind polypeptides of the invention are also encompassed by the invention. Polynucleotides encoding this polypeptide are also encompassed by the invention.

This gene is expressed primarily in T-cells and T-cell lymphomas.

Polynucleotides and polypeptides of the invention are useful as reagents for differential identification of the tissue(s) or cell type(s) present in a biological sample and for diagnosis of diseases and conditions which include, but are not limited to, immunological diseases involving T-cells such as inflammation, autoimmunity, and cancers including T-cell lymphomas. Similarly, polypeptides and antibodies directed to these polypeptides are useful in providing immunological probes for differential identification of the tissue(s) or cell type(s). For a number of disorders of the above tissues or cells, particularly of T-cells and other cells of the immune system, expression of this gene at significantly higher or lower levels may be routinely detected in certain tissues or cell types (e.g. immune, cancerous and wounded tissues)

or bodily fluids (e.g. lymph, serum, plasma, urine, synovial fluid and spinal fluid) or another tissue or cell sample taken from an individual having such a disorder, relative to the standard gene expression level, i.e., the expression level in healthy tissue or bodily fluid from an individual not having the disorder.

The tissue distribution in T-cells and T-cell lymphomas indicates that the protein product of this gene is useful for diagnosing and treating T-cell based disorders such as inflammatory diseases, autoimmune disease and tumors including T-cell lymphomas. Furthermore, the tissue distribution indicates that the polypeptides or polynucleotides are useful for the treatment, prophylaxis, and diagnosis of immune and autoimmune diseases, such as lupus, transplant rejection, allergic reactions, arthritis, asthma, immunodeficiency diseases, leukemia, and AIDS. Additionally, expression of this gene product in T cells also strongly indicates a role for this protein in immune function and immune surveillance. Protein, as well as, antibodies directed against the protein may show utility as a tumor marker and/or immunotherapy targets for the above listed tissues.

Many polynucleotide sequences, such as EST sequences, are publicly available and accessible through sequence databases. Some of these sequences are related to SEQ ID NO:14 and may have been publicly available prior to conception of the present invention. Preferably, such related polynucleotides are specifically excluded from the scope of the present invention. To list every related sequence is cumbersome. Accordingly, preferably excluded from the present invention are one or more polynucleotides comprising a nucleotide sequence described by the general formula of a-b, where a is any integer between 1 to 829 of SEQ ID NO:14, b is an integer of 15 to 843, where both a and b correspond to the positions of nucleotide residues shown in SEQ ID NO:14, and where b is greater than or equal to a + 14.

FEATURES OF PROTEIN ENCODED BY GENE NO: 5

This gene is expressed primarily in activated monocytes.

Polynucleotides and polypeptides of the invention are useful as reagents for differential identification of the tissue(s) or cell type(s) present in a biological sample

and for diagnosis of diseases and conditions which include, but are not limited to, inflammation, autoimmunity, infection, or disorders involving activation of monocytes. Similarly, polypeptides and antibodies directed to these polypeptides are useful in providing immunological probes for differential identification of the tissue(s) or cell type(s). For a number of disorders of the above tissues or cells, particularly of the immune system, expression of this gene at significantly higher or lower levels may be routinely detected in certain tissues or cell types (e.g. immune, cancerous and wounded tissues) or bodily fluids (e.g. lymph, serum, plasma, urine, synovial fluid and spinal fluid) or another tissue or cell sample taken from an individual having such a disorder, relative to the standard gene expression level, i.e., the expression level in healthy tissue or bodily fluid from an individual not having the disorder.

Predicted epitopes include those comprising a sequence shown in SEQ ID NO: 253 as residues: Asp-19 to Arg-31.

The tissue distribution indicates that the protein product of this gene is useful for diagnosing or treating diseases that result in activation of monocytes including infections, inflammatory responses or autoimmune diseases. Furthermore, expression of this gene product in monocytes also strongly indicates a role for this protein in immune function and immune surveillance.

Many polynucleotide sequences, such as EST sequences, are publicly available and accessible through sequence databases. Some of these sequences are related to SEQ ID NO:15 and may have been publicly available prior to conception of the present invention. Preferably, such related polynucleotides are specifically excluded from the scope of the present invention. To list every related sequence is cumbersome. Accordingly, preferably excluded from the present invention are one or more polynucleotides comprising a nucleotide sequence described by the general formula of a-b, where a is any integer between 1 to 1004 of SEQ ID NO:15, b is an integer of 15 to 1018, where both a and b correspond to the positions of nucleotide residues shown in SEQ ID NO:15, and where b is greater than or equal to a + 14.

FEATURES OF PROTEIN ENCODED BY GENE NO: 6

The translation product of this gene shares sequence homology with terminal deoxynucleotidyltransferase which is thought to be important in catalyzing the elongation of oligo- or polydeoxynucleotide chains.

In specific embodiments, polypeptides of the invention comprise, or alternatively consists of, the following amino acid sequence: FKKLVNPRXQGIRHEEEAVSWQERR (SEQ ID NO:490). Moreover, fragments and variants of this polypeptide (such as, for example, fragments as described herein, polypeptides at least 80%, 85%, 90%, 95%, 96%, 97%, 98%, or 99% identical to these polypeptides and polypeptides encoded by the polynucleotide which hybridize, under stringent conditions, to the polynucleotide encoding this polypeptide are encompassed by the invention. Antibodies that bind polypeptides of the invention are also encompassed by the invention. Polynucleotides encoding this polypeptide are also encompassed by the invention.

This gene is expressed primarily in activated human neutrophils, and to a lesser extent in T-cells, primary dendritic cells and bone marrow cells.

Polynucleotides and polypeptides of the invention are useful as reagents for differential identification of the tissue(s) or cell type(s) present in a biological sample and for diagnosis of diseases and conditions which include, but are not limited to, cancers, particularly those of the blood such as leukemia and deficiencies in neutrophils such as neutropenia, and immune system disorders. Similarly, polypeptides and antibodies directed to these polypeptides are useful in providing immunological probes for differential identification of the tissue(s) or cell type(s). For a number of disorders of the above tissues or cells, particularly of the cardiovascular and immune systems, expression of this gene at significantly higher or lower levels may be routinely detected in certain tissues or cell types (e.g. immune, cancerous and wounded tissues) or bodily fluids (e.g. lymph, serum, plasma, urine, synovial fluid and spinal fluid) or another tissue or cell sample taken from an individual having such a disorder, relative to the standard gene expression level, i.e., the expression level in healthy tissue or bodily fluid from an individual not having the disorder.

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The tissue distribution in neutrophils and other immune cells, combined with the homology to terminal deoxynucleotidyltransferase indicates that the protein product of this gene is useful for the treatment and differential diagnosis of acute leukemias. Alternatively, this gene may function in the proliferation of neutrophils and be useful as a treatment for neutropenia, for example, following neutropenia as a result of chemotherapy. Additionally, the tissue distribution indicates that the protein product of this gene is useful for the diagnosis and/or treatment of hematopoietic disorders. This gene product is primarily expressed in hematopoietic cells and tissues, suggesting that it plays a role in the survival, proliferation, and/or differentiation of hematopoietic lineages. This is particularly supported by the expression of this gene product in bone marrow, which is a primary site of definitive hematopoiesis. Expression of this gene product in T cells and primary dendritic cells also strongly indicates a role for this protein in immune function and immune surveillance.

Many polynucleotide sequences, such as EST sequences, are publicly available and accessible through sequence databases. Some of these sequences are related to SEQ ID NO:16 and may have been publicly available prior to conception of the present invention. Preferably, such related polynucleotides are specifically excluded from the scope of the present invention. To list every related sequence is cumbersome. Accordingly, preferably excluded from the present invention are one or more polynucleotides comprising a nucleotide sequence described by the general formula of a-b, where a is any integer between 1 to 647 of SEQ ID NO:16, b is an integer of 15 to 661, where both a and b correspond to the positions of nucleotide residues shown in SEQ ID NO:16, and where b is greater than or equal to a + 14.

FEATURES OF PROTEIN ENCODED BY GENE NO: 7

The translation product of this gene exhibits a reasonable homology to the human chorionic gonadotropic (HCG) analogue-GT beta-subunit as disclosed in U.S. Patent No. 5,508,261 and PCT Publication No. WO 92/22568. There is a high

degree of conservation of the structurally important cysteine residues between these proteins.

This gene is expressed primarily in IL-1 and LPS induced neutrophils.

Polynucleotides and polypeptides of the invention are useful as reagents for differential identification of the tissue(s) or cell type(s) present in a biological sample and for diagnosis of diseases and conditions which include, but are not limited to, diseases of the immune system, including inflammatory diseases and allergies. Similarly, polypeptides and antibodies directed to these polypeptides are useful in providing immunological probes for differential identification of the tissue(s) or cell type(s). For a number of disorders of the above tissues or cells, particularly of the immune system, expression of this gene at significantly higher or lower levels may be routinely detected in certain tissues or cell types (e.g., immune, cancerous and wounded tissues) or bodily fluids (e.g. lymph, serum, plasma, urine, synovial fluid and spinal fluid) or another tissue or cell sample taken from an individual having such a disorder, relative to the standard gene expression level, i.e., the expression level in healthy tissue or bodily fluid from an individual not having the disorder.

The tissue distribution in neutrophils indicates that the protein product of this gene is useful for the treatment/diagnosis of diseases of the immune system, since expression is primarily in neutrophils, and thus the translation product of this gene may be useful as a growth factor for the differentiation and/or proliferation of neutrophils for the treatment of neutropenia, for example following chemotherapy.

Many polynucleotide sequences, such as EST sequences, are publicly available and accessible through sequence databases. Some of these sequences are related to SEQ ID NO:17 and may have been publicly available prior to conception of the present invention. Preferably, such related polynucleotides are specifically excluded from the scope of the present invention. To list every related sequence is cumbersome. Accordingly, preferably excluded from the present invention are one or more polynucleotides comprising a nucleotide sequence described by the general formula of a-b, where a is any integer between 1 to 539 of SEQ ID NO:17, b is an integer of 15 to 553, where both a and b correspond to the positions of nucleotide residues shown in SEQ ID NO:17, and where b is greater than or equal to a + 14.

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FEATURES OF PROTEIN ENCODED BY GENE NO: 8

This gene is expressed primarily in IL-1 and LPS-induced neutrophils.

Polynucleotides and polypeptides of the invention are useful as reagents for differential identification of the tissue(s) or cell type(s) present in a biological sample and for diagnosis of diseases and conditions which include, but are not limited to, diseases of the immune system, including inflammatory diseases and allergies. Similarly, polypeptides and antibodies directed to these polypeptides are useful in providing immunological probes for differential identification of the tissue(s) or cell type(s). For a number of disorders of the above tissues or cells, particularly of the immune system, expression of this gene at significantly higher or lower levels may be routinely detected in certain tissues or cell types (e.g., immune, cancerous and wounded tissues) or bodily fluids (e.g. lymph, serum, plasma, urine, synovial fluid and spinal fluid) or another tissue or cell sample taken from an individual having such a disorder, relative to the standard gene expression level, i.e., the expression level in healthy tissue or bodily fluid from an individual not having the disorder.

Predicted epitopes include those comprising a sequence shown in SEQ ID NO: 256 as residues: Ser-14 to Pro-22, and/or Leu-43 to Val-53.

The tissue distribution in neutrophils indicates that the protein product of this gene is useful for the treatment and diagnosis of diseases of the immune system, since expression is primarily in neutrophils, and thus the translation product of this gene may be useful as a growth factor for the differentiation and/or proliferation of neutrophils for the treatment of neutropenia, for example following chemotherapy.

Many polynucleotide sequences, such as EST sequences, are publicly available and accessible through sequence databases. Some of these sequences are related to SEQ ID NO:18 and may have been publicly available prior to conception of the present invention. Preferably, such related polynucleotides are specifically excluded from the scope of the present invention. To list every related sequence is cumbersome. Accordingly, preferably excluded from the present invention are one or more polynucleotides comprising a nucleotide sequence described by the general formula of a-b, where a is any integer between 1 to 855 of SEQ ID NO:18, b is an

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integer of 15 to 869, where both a and b correspond to the positions of nucleotide residues shown in SEQ ID NO:18, and where b is greater than or equal to a + 14.

FEATURES OF PROTEIN ENCODED BY GENE NO: 9

When tested against Jurkat cell lines, supernatants removed from cells expressing this gene activated the NF-kB transcription factor. Thus, it is likely that the protein encoded by this gene activates Jurkat cells by activating a transcriptional factor found within these cells. Nuclear factor kB is a transcription factor activated by a wide variety of agents, leading to cell activation, differentiation, or apoptosis. Reporter constructs utilizing the NF-kB promoter element are used to screen supernatants for such activity.

This gene is expressed primarily in IL-1 and LPS induced neutrophils.

Polynucleotides and polypeptides of the invention are useful as reagents for differential identification of the tissue(s) or cell type(s) present in a biological sample and for diagnosis of diseases and conditions which include, but are not limited to, diseases of the immune system, including inflammatory diseases and allergies. Similarly, polypeptides and antibodies directed to these polypeptides are useful in providing immunological probes for differential identification of the tissue(s) or cell type(s). For a number of disorders of the above tissues or cells, particularly of the immune system, expression of this gene at significantly higher or lower levels may be routinely detected in certain tissues or cell types (e.g., immune, cancerous and wounded tissues) or bodily fluids (e.g. lymph, serum, plasma, urine, synovial fluid and spinal fluid) or another tissue or cell sample taken from an individual having such a disorder, relative to the standard gene expression level, i.e., the expression level in healthy tissue or bodily fluid from an individual not having the disorder.

Predicted epitopes include those comprising a sequence shown in SEQ ID NO: 257 as residues: Tyr-22 to His-35.

The tissue distribution in neutrophils, combined with the biological activity data suggest that the protein product of this gene is useful for the treatment and/or diagnosis of diseases of the immune system, since expression is primarily in

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neutrophils, and thus the translation product of this gene may be useful as a growth factor for the differentiation and/or proliferation of neutrophils for the treatment of neutropenia, for example following chemotherapy.

Many polynucleotide sequences, such as EST sequences, are publicly available and accessible through sequence databases. Some of these sequences are related to SEQ ID NO:19 and may have been publicly available prior to conception of the present invention. Preferably, such related polynucleotides are specifically excluded from the scope of the present invention. To list every related sequence is cumbersome. Accordingly, preferably excluded from the present invention are one or more polynucleotides comprising a nucleotide sequence described by the general formula of a-b, where a is any integer between 1 to 945 of SEQ ID NO:19, b is an integer of 15 to 959, where both a and b correspond to the positions of nucleotide residues shown in SEQ ID NO:19, and where b is greater than or equal to a + 14.

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FEATURES OF PROTEIN ENCODED BY GENE NO: 10

This gene is expressed primarily in activated T-cells and to a lesser extent in endothelial cells.

Polynucleotides and polypeptides of the invention are useful as reagents for differential identification of the tissue(s) or cell type(s) present in a biological sample and for diagnosis of diseases and conditions which include, but are not limited to, immune dysfunctions including cancer of the T lymphocytes and autoimmune disorders and inflammation. Similarly, polypeptides and antibodies directed to these polypeptides are useful in providing immunological probes for differential identification of the tissue(s) or cell type(s). For a number of disorders of the above tissues or cells, particularly of the immune system, expression of this gene at significantly higher or lower levels may be routinely detected in certain tissues or cell types (e.g. immune, cancerous and wounded tissues) or bodily fluids (e.g. lymph, serum, plasma, urine, synovial fluid and spinal fluid) or another tissue or cell sample

taken from an individual having such a disorder, relative to the standard gene expression level, i.e., the expression level in healthy tissue or bodily fluid from an individual not having the disorder.

The tissue distribution in activated T-cells indicates that the protein product of this gene is useful for the treatment and/or diagnosis of immune disorders, particularly of T-cell origin, and may act as a growth factor for particular subsets of T-cells such as CD4 positive cells, which would make this a useful therapeutic for the treatment of HIV and other immune compromising illnesses. Furthermore, this gene product may be involved in the regulation of cytokine production, antigen presentation, or other processes that may also suggest a usefulness in the treatment of AIDS or other immune compromising diseases (e.g. by boosting immune responses).

Many polynucleotide sequences, such as EST sequences, are publicly available and accessible through sequence databases. Some of these sequences are related to SEQ ID NO:20 and may have been publicly available prior to conception of the present invention. Preferably, such related polynucleotides are specifically excluded from the scope of the present invention. To list every related sequence is cumbersome. Accordingly, preferably excluded from the present invention are one or more polynucleotides comprising a nucleotide sequence described by the general formula of a-b, where a is any integer between 1 to 1432 of SEQ ID NO:20, b is an integer of 15 to 1446, where both a and b correspond to the positions of nucleotide residues shown in SEQ ID NO:20, and where b is greater than or equal to a + 14.

FEATURES OF PROTEIN ENCODED BY GENE NO: 11

The gene encoding the disclosed cDNA is thought to reside on chromosome 3. Accordingly, polynucleotides related to this invention are useful as a marker in linkage analysis for chromosome 3.

This gene is expressed primarily in fetal tissues, such as liver/spleen and brain, as well as in placental tissue.

Polynucleotides and polypeptides of the invention are useful as reagents for differential identification of the tissue(s) or cell type(s) present in a biological sample and for the diagnosis of many developmental abnormalities. Similarly, polypeptides

and antibodies directed to these polypeptides are useful in providing immunological probes for differential identification of the tissue(s) or cell type(s). For a number of disorders of the above tissues or cells, particularly of the developing fetus, expression of this gene at significantly higher or lower levels may be routinely detected in certain tissues or cell types (e.g. fetal, placental, cancerous and wounded tissues) or bodily fluids (e.g., lymph, serum, plasma, urine, synovial fluid and spinal fluid) or another tissue or cell sample taken from an individual having such a disorder, relative to the standard gene expression level, i.e., the expression level in healthy tissue or bodily fluid from an individual not having the disorder.

The tissue distribution in fetal tissues indicates that the protein product of this gene is useful as a growth factor or differentiation factor for particular cell types in the developing fetus and may be useful in replacement or other types of therapy in cases where the gene is expressed aberrantly. Furthermore, the tissue distribution indicates that the protein product of this gene is useful for the diagnosis and/or treatment of disorders of the placenta. Specific expression within the placenta indicates that this gene product may play a role in the proper establishment and maintenance of placental function. Alternately, this gene product may be produced by the placenta and then transported to the embryo, where it may play a crucial role in the development and/or survival of the developing embryo or fetus. Expression of this gene product in a vascular-rich tissue such as the placenta also indicates that this gene product may be produced more generally in endothelial cells or within the circulation. In such instances, it may play more generalized roles in vascular function, such as in angiogenesis. It may also be produced in the vasculature and have effects on other cells within the circulation, such as hematopoietic cells. It may serve to promote the proliferation, survival, activation, and/or differentiation of hematopoietic cells, as well as other cells throughout the body.

Many polynucleotide sequences, such as EST sequences, are publicly available and accessible through sequence databases. Some of these sequences are related to SEQ ID NO:21 and may have been publicly available prior to conception of the present invention. Preferably, such related polynucleotides are specifically excluded from the scope of the present invention. To list every related sequence is cumbersome. Accordingly, preferably excluded from the present invention are one or

more polynucleotides comprising a nucleotide sequence described by the general formula of a-b, where a is any integer between 1 to 1457 of SEQ ID NO:21, b is an integer of 15 to 1471, where both a and b correspond to the positions of nucleotide residues shown in SEQ ID NO:21, and where b is greater than or equal to a + 14.

FEATURES OF PROTEIN ENCODED BY GENE NO: 12

In specific embodiments, polypeptides of the invention comprise, or alternatively consists of, an amino acid sequence selected from the group: ISVLXYPHCVVHELPELTAESLEAGDSNQFCWRNLFSCINLLRILNKLTKWKH SRTMMLVVFKSAPILKRALKVKQAMMQLYVLKLLKVQTKYLGRQWRKSN MKTMSAIYQKVRHRLNDDWAYGNDLDARPWDFQAEECALRANIERFNARR YDRAHSNPDFLPVDNCLQSVLGQRVDLPEDFQMNYDLWLEREVFSKPISWEE LL (SEQ ID NO:491), MRAASPPASASDLIEQQQKRGRREHKALIKQDNLDAFNERD PYKADDSREEEEENDDDNSLEGETFPLERDEVMPPPLQHPQTDRLXCPKGLP WXPKVREKDIEMFLESSRSKFIGYTLGSDTNTVVGLPRPIHESIKTLKQHKYTS IAEVQAQMEEEYLRSPLSGGEEEVEQVPAETLYQGLLPSLPQYMIALLKILLA AAPTSKAKTDSINILADVLPEEMPTTVLQSMKLGVDVNRHKEVIVKAISAVLL LLLKHFKLNHVYQFEYMAQHLVFANCIPLILKFFNQNIMSYITAKNSISVLDYP HCVVHELPELTAESLEAGDSNQFCWRNLFSCINLLRILNKLTKWKHSRTMML VVFKSAPILKRALKVKQAMMQLYVLKLLKVQTKYLGRQWRKSNMKTMSAI YQKVRHRLNDDWAYGNDLDARPWDFQAEECALRANIERFNARRYDRAHSN PDFLPVDNCLQSVLGQRVDLPEDFQMNYDLWLEREVFSKPISWEELLQ (SEQ ID NO:492), MRAASPPASASDLIEQQQKRGRREHKALIKQDNLDAFNERDPYKADDSRE (SEQ ID NO:493), EEEENDDDNSLEGETFPLERDEVMPPPLQHPQTDRLX CPKGLPWX (SEQ ID NO:494), PKVREKDIEMFLESSRSKFIGYTLGSDTNTV VGLPRPIHESIKTLKQHKYT (SEQ ID NO:495), SIAEVQAQMEEEYLRSPLSGG EEEVEQVPAETLYQGLLPSLPQYMIA (SEQ ID NO:496), LLKILLAAAPTSKAK TDSINILADVLPEEMPTTVLQSMKLGVDVNRHK (SEQ ID NO:497), EVIVKA

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ISAVLLLLLKHFKLNHVYQFEYMAQHLVFANCIPLILKFFNQNI (SEQ ID NO:498), MSYITAKNSISVLDYPHCVVHELPELTAESLEAGDSNQFCWRNLFSCI (SEQ ID NO:499), NLLRILNKLTKWKHSRTMMLVVFKSAPILKRALKVKQ AMMQLYVLKL (SEQ ID NO:500), LKVQTKYLGRQWRKSNMKTMSAIYQKVRH RLNDDWAYGNDLDARP (SEQ ID NO:501), WDFQAEECALRANIERFNARRYDR AHSNPDFLPVDNCLQSVLGQRVDL (SEQ ID NO:502), and PEDFQMNYDLWLE REV FSKPISWEELLQ (SEQ ID NO:503). Moreover, fragments and variants of these polypeptides (such as, for example, fragments as described herein, polypeptides at least 80%, 85%, 90%, 95%, 96%, 97%, 98%, or 99% identical to these polypeptides and polypeptides encoded by the polynucleotide which hybridizes, under stringent conditions, to the polynucleotide encoding these polypeptides) are encompassed by the invention. Antibodies that bind polypeptides of the invention are also encompassed by the invention. Polynucleotides encoding these polypeptides are also encompassed by the invention.

The translation product of this gene shares sequence homology with a C. elegans protein (gi|1086830 coded for by C. elegans cDNA yk20f8.5).

This gene is expressed primarily in T-cells, and to a lesser extent in tumor tissue including glioblastoma, menangioma, and Wilm's tumor.

Polynucleotides and polypeptides of the invention are useful as reagents for differential identification of the tissue(s) or cell type(s) present in a biological sample and for diagnosis of diseases and conditions which include, but are not limited to, diseases of the immune system, including autoimmune conditions such as rheumatoid arthritis, inflammatory disorders and cancer. Similarly, polypeptides and antibodies directed to these polypeptides are useful in providing immunological probes for differential identification of the tissue(s) or cell type(s). For a number of disorders of the above tissues or cells, particularly of the immune system, expression of this gene at significantly higher or lower levels may be routinely detected in certain tissues or cell types (e.g. immune, cancerous and wounded tissues) or bodily fluids (e.g. lymph, serum, plasma, urine, synovial fluid and spinal fluid) or another tissue or cell sample taken from an individual having such a disorder, relative to the standard gene

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expression level, i.e., the expression level in healthy tissue or bodily fluid from an individual not having the disorder.

Predicted epitopes include those comprising a sequence shown in SEQ ID NO: 260 as residues: Thr-9 to Ser-14.

The tissue distribution in T-cells indicates that the protein product of this gene is useful for the diagnosis and/or modulation of immune function disorders, including rheumatoid arthritis and inflammatory responses. Furthermore, this gene product may be involved in the regulation of cytokine production, antigen presentation, or other processes that may also suggest a usefulness in the treatment of cancer (e.g. by boosting immune responses). Since the gene is expressed in cells of lymphoid origin, the gene or protein, as well as, antibodies directed against the protein may show utility as a tumor marker and/or immunotherapy targets for the above listed tissues. Expression of this gene product in T cells also strongly indicates a role for this protein in immune function and immune surveillance.

Many polynucleotide sequences, such as EST sequences, are publicly available and accessible through sequence databases. Some of these sequences are related to SEQ ID NO:22 and may have been publicly available prior to conception of the present invention. Preferably, such related polynucleotides are specifically excluded from the scope of the present invention. To list every related sequence is cumbersome. Accordingly, preferably excluded from the present invention are one or more polynucleotides comprising a nucleotide sequence described by the general formula of a-b, where a is any integer between 1 to 1388 of SEQ ID NO:22, b is an integer of 15 to 1402, where both a and b correspond to the positions of nucleotide residues shown in SEQ ID NO:22, and where b is greater than or equal to a + 14.

FEATURES OF PROTEIN ENCODED BY GENE NO: 13

This gene is expressed primarily in placenta, and to a lesser extent in fetal liver and bone marrow.

Polynucleotides and polypeptides of the invention are useful as reagents for differential identification of the tissue(s) or cell type(s) present in a biological sample

and for the diagnosis of hematological disorders. Similarly, polypeptides and antibodies directed to these polypeptides are useful in providing immunological probes for differential identification of the tissue(s) or cell type(s). For a number of disorders of the above tissues or cells, particularly of the hematological and immune systems, expression of this gene at significantly higher or lower levels may be routinely detected in certain tissues or cell types (e.g. placental, immune, cancerous and wounded tissues) or bodily fluids (e.g. lymph, serum, plasma, urine, synovial fluid and spinal fluid) or another tissue or cell sample taken from an individual having such a disorder, relative to the standard gene expression level, i.e., the expression level in healthy tissue or bodily fluid from an individual not having the disorder.

The tissue distribution in fetal liver, and bone marrow indicates that the protein product of this gene is useful as a growth factor for hematopoietic stem cells or progenitor cells in the treatment of chemotherapy patients or kidney disease. Furthermore, the tissue distribution in placenta indicates that the protein product of this gene is useful for the diagnosis and/or treatment of vascular or reproductive disorders. Specific expression within the placenta indicates that this gene product may play a role in the proper establishment and maintenance of placental function. Alternately, this gene product may be produced by the placenta and then transported to the embryo, where it may play a crucial role in the development and/or survival of the developing embryo or fetus. Expression of this gene product in a vascular-rich tissue such as the placenta also indicates that this gene product may be produced more generally in endothelial cells or within the circulation. In such instances, it may play more generalized roles in vascular function, such as in angiogenesis. It may also be produced in the vasculature and have effects on other cells within the circulation, such as hematopoietic cells. It may serve to promote the proliferation, survival, activation, and/or differentiation of hematopoietic cells, as well as other cells throughout the body.

Many polynucleotide sequences, such as EST sequences, are publicly available and accessible through sequence databases. Some of these sequences are related to SEQ ID NO:23 and may have been publicly available prior to conception of the present invention. Preferably, such related polynucleotides are specifically excluded from the scope of the present invention. To list every related sequence is

cumbersome. Accordingly, preferably excluded from the present invention are one or more polynucleotides comprising a nucleotide sequence described by the general formula of a-b, where a is any integer between 1 to 1033 of SEQ ID NO:23, b is an integer of 15 to 1047, where both a and b correspond to the positions of nucleotide residues shown in SEQ ID NO:23, and where b is greater than or equal to a + 14.

FEATURES OF PROTEIN ENCODED BY GENE NO: 14

This gene is expressed primarily in stromal cells.

Polynucleotides and polypeptides of the invention are useful as reagents for differential identification of the tissue(s) or cell type(s) present in a biological sample and for diagnosis of hematopoietic disorders including cancer, neutropenia, anemia, and thrombocytopenia. Similarly, polypeptides and antibodies directed to these polypeptides are useful in providing immunological probes for differential identification of the tissue(s) or cell type(s). For a number of disorders of the above tissues or cells, particularly of the hematopoietic and immune systems, expression of this gene at significantly higher or lower levels may be routinely detected in certain tissues or cell types (e.g. immune, cancerous and wounded tissues) or bodily fluids (e.g. lymph, serum, plasma, urine, synovial fluid and spinal fluid) or another tissue or cell sample taken from an individual having such a disorder, relative to the standard gene expression level, i.e., the expression level in healthy tissue or bodily fluid from an individual not having the disorder.

The tissue distribution in stromal cells indicates that the protein product of this gene is useful as a growth factor for hematopoietic stem cells or progenitor cells, in particular following chemotherapy treatment. Furthermore, the tissue distribution indicates that the protein product of this gene is useful for the treatment and diagnosis of hematopoetic related disorders such as anemia, pancytopenia, leukopenia, thrombocytopenia or leukemia, since stromal cells are important in the production of cells of hematopoietic lineages. The uses include bone marrow cell ex vivo culture, bone marrow transplantation, bone marrow reconstitution, radiotherapy or chemotherapy of neoplasia. The gene product may also be involved in

lymphopoiesis, therefore, it can be used in immune disorders such as infection, inflammation, allergy, immunodeficiency etc. In addition, this gene product may have commercial utility in the expansion of stem cells and committed progenitors of various blood lineages, and in the differentiation and/or proliferation of various cell types.

Many polynucleotide sequences, such as EST sequences, are publicly available and accessible through sequence databases. Some of these sequences are related to SEQ ID NO:24 and may have been publicly available prior to conception of the present invention. Preferably, such related polynucleotides are specifically excluded from the scope of the present invention. To list every related sequence is cumbersome. Accordingly, preferably excluded from the present invention are one or more polynucleotides comprising a nucleotide sequence described by the general formula of a-b, where a is any integer between 1 to 976 of SEQ ID NO:24, b is an integer of 15 to 990, where both a and b correspond to the positions of nucleotide residues shown in SEQ ID NO:24, and where b is greater than or equal to a + 14.

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FEATURES OF PROTEIN ENCODED BY GENE NO: 15

The translation product of this gene shares sequence homology with epsilon-COP from Bos taurus, which is thought to be important as a component of coatomer, a complex of seven proteins, that is the major component of the non-clathrin membrane coat.

In specific embodiments, polypeptides of the invention comprise, or alternatively consists of, an amino acid sequence selected from the group: MAPPAPGPASGGSGEVDELFDVKNAFYIGSYQQCINEAXXVKLSSPERDVER DVFLYRAYLAQRKFGVVLDEIKPSSAPELQAVRMFADYLAHESRRDSIVAEL DREMSRSXDVTNTTFLLMAASIYLHDQNPDAALRALHQGDSLECTAMTVQIL LKLDRLDLARKELKRMQDLDEDATLTQLATAWVSLATGGEKLQDAYYIFQE MADKCSPTLLLLNGQAACHMAQGRWEAAEGLLQEALDKDSGYPETLVNLIV LSQHLGKPPEVTNRYLSQLKDAHRSHPFIKEYQAKENDFDRLVLQYAPSAEA GPELSGP (SEQ ID NO:504),

RDVERDVFLYRAYLAQRKFGVVLDEIKPSSAPELQAVRMFADYLAHESRRDS IVAELDREMSRSXDVTNTTFLLMAASIYLHDQNPDAALRALHQGDSLECTAM TVQILLKLDRLDLARKELKRMQDLDEDATLTQLATAWVSLATGGEKLQDAY YIFQEMADKCSPTLLLLNGQAACHMAQGRWEAAEGLLQEALDKDSGYPETL VNLIVLSQHLGKPPEVTNRYLSQLKDAHRSHPFIKEYQAKENDFDRLVLQYA PSA (SEQ ID NO:505),

MAPPAPGPASGGSGEVDELFDVKNAFYIGSYQQCINEAXXVKLSSPER (SEQ ID NO:506),

DVERDVFLYRAYLAQRKFGVVLDEIKPSSAPELQAVRMFADYLAHES (SEQ ID NO:507),

RRDSIVAELDREMSRSXDVTNTTFLLMAASIYLHDQNPDAALRALHQG (SEQ ID NO:508),

DSLECTAMTVQILLKLDRLDLARKELKRMQDLDEDATLTQLATAWVS (SEQ ID NO:509),

LATGGEKLQDAYYIFQEMADKCSPTLLLLNGQAACHMAQGRWEAAEG (SEQ ID NO:510),

LLQEALDKDSGYPETLVNLIVLSQHLGKPPEVTNRYLSQLKDAHRSHP (SEQ ID NO:511), FIKEYQAKENDFDRLVLQYAPSAEAGPELSGP (SEQ ID NO:512), RDVERDVFLYRAYLAQRKFGVVLDEIKPSSAPELQAVRMFADYLAHE (SEQ ID NO:513),

SRRDSIVAELDREMSRSXDVTNTTFLLMAASIYLHDQNPDAALRALHQ (SEQ ID NO:514),

GDSLECTAMTVQILLKLDRLDLARKELKRMQDLDEDATLTQLATAWV (SEQ ID NO:515),

SLATGGEKLQDAYYIFQEMADKCSPTLLLLNGQAACHMAQGRWEAAE (SEQ ID NO:516), GLLQEALDKDSG YPETLVNLIVLSQHLGKPPEVTNRYL (SEQ ID NO:517), SQLKDAHRSHPFIKEYQAKENDFDRLVLQYAPSA (SEQ ID NO:518), or

NRYYRESWSLQVPVRNSGSTHASERNGASGPRPGLRRLRGGRRAVRRKERL LHRQLPAVHKR (SEQ ID NO:519). Moreover, fragments and variants of these polypeptides (such as, for example, fragments as described herein, polypeptides at least 80%, 85%, 90%, 95%, 96%, 97%, 98%, or 99% identical to these polypeptides

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and polypeptides encoded by the polynucleotide which hybridizes, under stringent conditions, to the polynucleotide encoding these polypeptides) are encompassed by the invention. Antibodies that bind polypeptides of the invention are also encompassed by the invention. Polynucleotides encoding these polypeptides are also encompassed by the invention.

The gene encoding the disclosed cDNA is thought to reside on chromosome 19. Accordingly, polynucleotides of the invention are useful as a marker in linkage analysis for chromosome 19.

This gene is expressed primarily in activated monocytes and T-cells.

Polynucleotides and polypeptides of the invention are useful as reagents for differential identification of the tissue(s) or cell type(s) present in a biological sample and for diagnosis of diseases and conditions which include, but are not limited to, immunomodulation, specifically relating to transport problems in these cells. Similarly, polypeptides and antibodies directed to these polypeptides are useful in providing immunological probes for differential identification of the tissue(s) or cell type(s). For a number of disorders of the above tissues or cells, particularly of the immune system, expression of this gene at significantly higher or lower levels may be routinely detected in certain tissues or cell types (e.g. immune, cancerous and wounded tissues) or bodily fluids (e.g. lymph, serum, plasma, urine, synovial fluid and spinal fluid) or another tissue or cell sample taken from an individual having such a disorder, relative to the standard gene expression level, i.e., the expression level in healthy tissue or bodily fluid from an individual not having the disorder.

The tissue distribution in activated monocytes and T-cells combined with the homology to epsilon-COP indicates that the protein product of this gene is useful for treating and/or diagnosing problems with the cellular transport of proteins that may result in immunologic dysfunction. Furthermore, this gene product may be involved in the regulation of cytokine production, antigen presentation, or other processes that may also suggest a usefulness in the treatment of cancer (e.g. by boosting immune responses). Since the gene is expressed in cells of lymphoid origin, the gene or protein, as well as, antibodies directed against the protein may show utility as a tumor marker and/or immunotherapy targets for the above listed tissues.

Many polynucleotide sequences, such as EST sequences, are publicly available and accessible through sequence databases. Some of these sequences are related to SEQ ID NO:25 and may have been publicly available prior to conception of the present invention. Preferably, such related polynucleotides are specifically excluded from the scope of the present invention. To list every related sequence is cumbersome. Accordingly, preferably excluded from the present invention are one or more polynucleotides comprising a nucleotide sequence described by the general formula of a-b, where a is any integer between 1 to 1194 of SEQ ID NO:25, b is an integer of 15 to 1208, where both a and b correspond to the positions of nucleotide residues shown in SEQ ID NO:25, and where b is greater than or equal to a + 14.

D0D3W2 <DOCID> WO 00/37626 PCT/US99/30

FEATURES OF PROTEIN ENCODED BY GENE NO: 16

The translation product of this gene shares sequence homology with an RNA helicase which is thought to be important in polynucleotide metabolism. The translation product of this contig exhibits good homology to the LbeIF4A antigen of Leishmania braziliensis. The LbeIF4A antigen, or immunogenic portions of it, can be used to induce protective immunity against leishmaniasis, specifically L. donovani, L. chagasi, L. infantum, L. major, L. braziliensis, L. panamensis, L. tropica and L. guyanensis. It can also be used diagnostically to detect Leishmania infection or to stimulate a cellular and/or humoral immune response or to stimulate the production of interleukin-12. The gene encoding the disclosed cDNA is thought to reside on chromosome 7. Accordingly, polynucleotides related to this invention are useful as a marker in linkage analysis for chromosome 7.

This gene is expressed primarily in colon cancer, and to a lesser extent, in pituitary.

Polynucleotides and polypeptides of the invention are useful as reagents for differential identification of the tissue(s) or cell type(s) present in a biological sample and for diagnosis of cancers particularly of the colon. Similarly, polypeptides and antibodies directed to these polypeptides are useful in providing immunological probes for differential identification of the tissue(s) or cell type(s). For a number of

disorders of the above tissues or cells, particularly of the gastrointestinal system, expression of this gene at significantly higher or lower levels may be routinely detected in certain tissues or cell types (e.g. colon, pituitary, cancerous and wounded tissues) or bodily fluids (e.g. lymph, serum, plasma, urine, synovial fluid and spinal fluid) or another tissue or cell sample taken from an individual having such a disorder, relative to the standard gene expression level, i.e., the expression level in healthy tissue or bodily fluid from an individual not having the disorder.

Predicted epitopes include those comprising a sequence shown in SEQ ID NO: 264 as residues: Glu-93 to Ala-98, Gln-150 to Leu-156, Leu-220 to Leu-231, Leu-268 to Arg-273, Val-324 to Pro-341, Arg-372 to Asn-380, Ser-405 to Gly-410, Phe-426 to Ala-433, Glu-458 to Asp-470, and/or Arg-506 to Ser-547.

The tissue distribution in colon cancer, combined with the homology to RNA helicase indicates that the protein product of this gene is useful for the development of diagnostic tests for colon cancer or other gastrointestinal or metabolic disorders. Protein, as well as, antibodies directed against the protein may show utility as a tissue-specific marker and/or immunotherapy target for the above listed tissues.

Many polynucleotide sequences, such as EST sequences, are publicly available and accessible through sequence databases. Some of these sequences are related to SEQ ID NO:26 and may have been publicly available prior to conception of the present invention. Preferably, such related polynucleotides are specifically excluded from the scope of the present invention. To list every related sequence is cumbersome. Accordingly, preferably excluded from the present invention are one or more polynucleotides comprising a nucleotide sequence described by the general formula of a-b, where a is any integer between 1 to 1908 of SEQ ID NO:26, b is an integer of 15 to 1922, where both a and b correspond to the positions of nucleotide residues shown in SEQ ID NO:26, and where b is greater than or equal to a + 14.

FEATURES OF PROTEIN ENCODED BY GENE NO: 17

PF-0822-PCT

The translation product of this contig has sequence homology to a cytoplasmic protein that binds specifically to JNK, designated the JNK interacting protein-1 or JIP-1 in Mus musculus. JIP-1 caused cytoplasmic retention of JNK and inhibition of JNK-regulated gene expression. The gene encoding the disclosed cDNA is thought to reside on chromosome 11. Accordingly, polynucleotides related to this invention are useful as a marker in linkage analysis for chromosome 11.

In specific embodiments, polypeptides of the invention comprise, or alternatively consists of, an amino acid sequence selected from the group: APGXGWRGSLGEPPPPPRASLSSDTSALSYDSVKYTLVVDEHAQLELV SLRRASETTVTRVTLPPS (SEQ ID NO:520), APGXGWRGSLGEPPPPPRASLSSDTSALSY (SEQ ID NO:521), or DSVKYTLVVDEHAQLELVSLRRASETTVTRVTLPPS (SEQ ID NO:522). Moreover, fragments and variants of these polypeptides (such as, for example, fragments as described herein, polypeptides at least 80%, 85%, 90%, 95%, 96%, 97%, 98%, or 99% identical to these polypeptides and polypeptides encoded by the polynucleotide which hybridizes, under stringent conditions, to the polynucleotide encoding these polypeptides) are encompassed by the invention. Antibodies that bind polypeptides of the invention are also encompassed by the invention. Polynucleotides encoding these polypeptides are also encompassed by the invention.

This gene is expressed primarily in brain, including pituitary, cerebellum, frontal cortex, and fetal brain, and to a lesser extent in the cortex or the kidney.

Polynucleotides and polypeptides of the invention are useful as reagents for differential identification of the tissue(s) or cell type(s) present in a biological sample and for diagnosis of the central nervous system disorders including ischemia, epilepsy, Parkinson's disease, and schizophrenia. Similarly, polypeptides and antibodies directed to these polypeptides are useful in providing immunological probes for differential identification of the tissue(s) or cell type(s). For a number of disorders of the above tissues or cells, particularly of the central nervous system, expression of this gene at significantly higher or lower levels may be routinely detected in certain tissues or cell types (e.g. brain, kidney, cancerous and wounded tissues) or bodily fluids (e.g. lymph, serum, plasma, urine, synovial fluid and spinal fluid) or another tissue or cell sample taken from an individual having such a

DOCKET NO: 2000.0050

disorder, relative to the standard gene expression level, i.e., the expression level in healthy tissue or bodily fluid from an individual not having the disorder. Furthermore, the translation product of this contig may suppress the effects of the JNK signaling pathway on cellular proliferation, including transformation by the Bcr-Abl oncogene.

Predicted epitopes include those comprising a sequence shown in SEQ ID NO: 265 as residues: Pro-6 to Ser-26, Ala-30 to Asp-41, Gly-55 to Ser-61, Gly-74 to Thr-80, Tyr-117 to Ala-123, Tyr-167 to Asp-172, Ala-212 to Cys-223, and/or Pro-239 to Tyr-244.

The tissue distribution in brain indicates that the protein product of this gene is useful for the enhanced survival and/or differentiation of neurons as a treatment for neurodegenerative disease. Furthermore, the tissue distribution indicates that the translation product of this gene may be involved in neuronal survival; synapse formation; conductance; neural differentiation, etc. Such involvement may impact many processes, such as learning and cognition. It may also be useful in the treatment of such neurodegenerative disorders as schizophrenia; ALS; or Alzheimer's.

Many polynucleotide sequences, such as EST sequences, are publicly available and accessible through sequence databases. Some of these sequences are related to SEQ ID NO:27 and may have been publicly available prior to conception of the present invention. Preferably, such related polynucleotides are specifically excluded from the scope of the present invention. To list every related sequence is cumbersome. Accordingly, preferably excluded from the present invention are one or more polynucleotides comprising a nucleotide sequence described by the general formula of a-b, where a is any integer between 1 to 1937 of SEQ ID NO:27, b is an integer of 15 to 1951, where both a and b correspond to the positions of nucleotide residues shown in SEQ ID NO:27, and where b is greater than or equal to a + 14.

FEATURES OF PROTEIN ENCODED BY GENE NO: 18

The translation product of this gene shares sequence homology with a liver stage antigen from a protozoan parasite.

This gene is expressed primarily in fetal tissue, and to a lesser extent, in activated T-cells and other immune cells.

Polynucleotides and polypeptides of the invention are useful as reagents for differential identification of the tissue(s) or cell type(s) present in a biological sample and for diagnosis of diseases and conditions which include, but are not limited to, developmental abnormalities and diseases of immune function. Similarly, polypeptides and antibodies directed to these polypeptides are useful in providing immunological probes for differential identification of the tissue(s) or cell type(s). For a number of disorders of the above tissues or cells, particularly of the immune system, expression of this gene at significantly higher or lower levels may be routinely detected in certain tissues or cell types (e.g. immune, cancerous and wounded tissues) or bodily fluids (e.g. lymph, serum, plasma, urine, synovial fluid and spinal fluid) or another tissue or cell sample taken from an individual having such a disorder, relative to the standard gene expression level, i.e., the expression level in healthy tissue or bodily fluid from an individual not having the disorder.

The tissue distribution in T-cells, combined with the homology to a protozoan antigen indicates that the protein product of this gene is useful for the treatment and/or immune modulation of parasitic infections. Furthermore, expression of this gene product in T cells also strongly indicates a role for this protein in immune function and immune surveillance.

Many polynucleotide sequences, such as EST sequences, are publicly available and accessible through sequence databases. Some of these sequences are related to SEQ ID NO:28 and may have been publicly available prior to conception of the present invention. Preferably, such related polynucleotides are specifically excluded from the scope of the present invention. To list every related sequence is cumbersome. Accordingly, preferably excluded from the present invention are one or more polynucleotides comprising a nucleotide sequence described by the general formula of a-b, where a is any integer between 1 to 3975 of SEQ ID NO:28, b is an integer of 15 to 3989, where both a and b correspond to the positions of nucleotide residues shown in SEQ ID NO:28, and where b is greater than or equal to a + 14.

WO 00/24764 PCT/US99/24764

FEATURES OF PROTEIN ENCODED BY GENE NO: 19

In specific embodiments, polypeptides of the invention comprise, or alternatively consists of, an amino acid sequence selected from the group: MKAIGIEPSLATYHHIIRLFDQPGDPLKRSSFIIYDIMNELMGKRFSPKDPDDD KFFQSAMSICSSLRDLELAYQVHGLLKTGDNWKFIGPDQHRNFYYSKFFDLIC LMEQIDVTLKWYEDLIPSAYFPHSQTMIHLLQALDVANRLEVIPKIWER (SEQ ID NO:523), KDSKEYGHTFRSDLREEILMLMARDKHPPELQVAFADCAADIKSAYESQPIRQ TAQDWPATSLNCIAILFLRAGRTQEAWKMLGLFRKHNKIPRSELLNELMDSA KVSNSPSQAIEVVELASAFSLPICEGLTQRVMSDFAINQEQKEALSNLTALTSD SDTDSSSDSDSDTSEGK (SEQ ID NO:524), MKAIGIEPSLATYHHIIRLFDQPGDPLKRSSFIIYDIMNELMGKRFSPK (SEQ ID NO:525), DPDDDKFFQSAMSICSSLRDLELAYQVHGLLKTGDNWKFIGPDQHRNFY (SEQ ID NO:526), YSKFFDLICLMEQIDVTLKWYEDLIPSA (SEQ ID NO:527), YFPHSQTMIHLLQALDVANRLEVIPKIWER (SEQ ID NO:528), KDSKEYGHTFRSDLREEILMLMARDKHPPELQVAFADCAADIKSAY (SEQ ID NO:529), ESQPIRQTAQDWPATSLNCIAILFLRAGRTQEAWKMLGLFRKHNKIPRSE (SEQ ID NO:530), LLNELMDSAKVSNSPSQAIEVVELASAFSLPICEGLTQRVMSDFAIN (SEQ ID NO:531), or QEQKEALSNLTALTSDSDTDSSSDSDSDTSEGK (SEQ ID NO:532). Moreover, fragments and variants of these polypeptides (such as, for example, fragments as described herein, polypeptides at least 80%, 85%, 90%, 95%, 96%, 97%, 98%, or 99% identical to these polypeptides and polypeptides encoded by the polynucleotide which hybridizes, under stringent conditions, to the polynucleotide encoding these polypeptides) are encompassed by the invention. Antibodies that bind polypeptides of the invention are also encompassed by the invention. Polynucleotides encoding these polypeptides are also encompassed by the invention.

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The gene encoding the disclosed cDNA is thought to reside on chromosome 2. Accordingly, polynucleotides related to this invention are useful as a marker in linkage analysis for chromosome 2.

This gene is expressed primarily in stromal and CD34 depleted bone marrow cells, and to a lesser extent in tissues of embryonic origin.

Polynucleotides and polypeptides of the invention are useful as reagents for differential identification of the tissue(s) or cell type(s) present in a biological sample and for diagnosis of diseases and conditions which include, but are not limited to, diseases of hematopoietic origin including cancers and immune dysfunction. Similarly, polypeptides and antibodies directed to these polypeptides are useful in providing immunological probes for differential identification of the tissue(s) or cell type(s). For a number of disorders of the above tissues or cells, particularly of the hematopoietic and immune systems, expression of this gene at significantly higher or lower levels may be routinely detected in certain tissues or cell types (e.g. immune, cancerous and wounded tissues) or bodily fluids (e.g. lymph, serum, plasma, urine, synovial fluid and spinal fluid) or another tissue or cell sample taken from an individual having such a disorder, relative to the standard gene expression level, i.e., the expression level in healthy tissue or bodily fluid from an individual not having the disorder.

WO 98/37207 PCT/US98/02804

Predicted epitopes include those comprising a sequence shown in SEQ ID NO: 267 as residues: Ser-28 to Gln-34.

The tissue distribution in stromal and CD34 depleted bone marrow cells indicates that the protein product of this gene is useful as a growth factor for hematopoietic stem cells or progenitor cells which may be useful in the treatment of chemotherapy patients suffering from neutropenia. Furthermore, the tissue distribution indicates that the protein product of this gene is useful for the treatment and diagnosis of hematopoetic related disorders such as anemia, pancytopenia, leukopenia, thrombocytopenia or leukemia, since stromal cells are important in the production of cells of hematopoietic lineages. The uses include bone marrow cell ex vivo culture, bone marrow transplantation, bone marrow reconstitution, radiotherapy or chemotherapy of neoplasia. The gene product may also be involved in lymphopoiesis, therefore, it can be used in immune disorders such as infection,

inflammation, allergy, immunodeficiency etc. In addition, this gene product may have commercial utility in the expansion of stem cells and committed progenitors of various blood lineages, and in the differentiation and/or proliferation of various cell types.

Many polynucleotide sequences, such as EST sequences, are publicly available and accessible through sequence databases. Some of these sequences are related to SEQ ID NO:29 and may have been publicly available prior to conception of the present invention. Preferably, such related polynucleotides are specifically excluded from the scope of the present invention. To list every related sequence is cumbersome. Accordingly, preferably excluded from the present invention are one or more polynucleotides comprising a nucleotide sequence described by the general formula of a-b, where a is any integer between 1 to 3721 of SEQ ID NO:29, b is an integer of 15 to 3735, where both a and b correspond to the positions of nucleotide residues shown in SEQ ID NO:29, and where b is greater than or equal to a + 14.

Docket No. 2002-0622

FEATURES OF PROTEIN ENCODED BY GENE NO: 20

In specific embodiments, polypeptides of the invention comprise, or alternatively consists of, an amino acid sequence selected from the group:
MSSDNESDIEDEDLKLELRRLRDKHLKEIQDLQSRQKHEIESLYTKLGKVPPA
VIIPPAAPLSGRRRRPTKSKGSKSSRSSSLGNKSPQLSGNLSGQSAASVLHPQQ
TLHPPGNIPESGQNQLLQPLKPSPSSDNLYSAFTSDGAISVPSLSAPGQGTSSTN
TVGATVNSQAAQAQPPAMTSSRKGTFTDDLHKLVDNWARDAMNLSGRRGS
KGHMNYEGPGMARKFSAPGQLCISMTSNLGGSAPISAASATSLGHFTKSMCP
PQQYGFPATPFGAQWSGTGGPAPQPLGQFQPVGTASLQNFNISNLQKSISNPP
GSNLRTT (SEQ ID NO:533),
IQDLQSRQKHEIESLYTKLGKVPPAVIIPPAAPLSGRRRRPTKSKGSKSSRSSSL
GNKSPQLSGNLSGQSAASVLHPQQTLHPPGNIPESGQNQLLQPLKPSPSSDNL
YSAFTSDGAISVPSLSAPGQGT SST (SEQ ID NO:534),
TSDGAISVPSLSAPGQGTSSTNTVGATVNSQAAQAQPPAMTSSRKGTFTDDL
H (SEQ ID NO:535),

KGHMNYEGPGMARKFSAPGQLCISMTSNLGGSAPISAASATSLGHFTK (SEQ ID NO:536), QPLKPSPSSDNL YSAFTSDGAISVPSLSAPG (SEQ ID NO:537), MSSDNESDIEDEDLKLELRRLRD KHLKEIQDLQSRQKHEIESLYTKLGKVP (SEQ ID NO:538),

PAVIIPPAAPLSGRRRRPTKSKGSKSSRSSSLGNKSPQLSGNLSGQS (SEQ ID NO:539),

AASVLHPQQTLHPPGNIPESGQNQLLQPLKPSPSSDNLYSAFTSDGAISV (SEQ ID NO:540), PSLSAPGQGTSSTNTVGATVNSQAAQAQPPAMTSSRKGTFTDDL (SEQ ID NO:541),

HKLVDNWARDAMNLSGRRGSKGHMNYEGPGMARKFSAPGQLCISMT (SEQ ID NO:542),

SNLGGSAPISAASATSLGHFTKSMCPPQQYGFPATPFGAQWSGTGG (SEQ ID NO:543), and PAPQPLGQFQPVGTASLQNFNISNLQKSISNPPGSNLRTT (SEQ ID NO:544). Moreover, fragments and variants of these polypeptides (such as, for example, fragments as described herein, polypeptides at least 80%, 85%, 90%, 95%, 96%, 97%, 98%, or 99% identical to these polypeptides and polypeptides encoded by the polynucleotide which hybridizes, under stringent conditions, to the polynucleotide encoding these polypeptides) are encompassed by the invention. Antibodies that bind polypeptides of the invention are also encompassed by the invention. Polynucleotides encoding these polypeptides are also encompassed by the invention.

This gene is expressed in fetal liver and tissues associated with the CNS.

Polynucleotides and polypeptides of the invention are useful as reagents for differential identification of the tissue(s) or cell type(s) present in a biological sample and for diagnosis of diseases and conditions which include, but are not limited to, liver and CNS diseases. Similarly, polypeptides and antibodies directed to these polypeptides are useful in providing immunological probes for differential identification of the tissue(s) or cell type(s). For a number of disorders of the above tissues or cells, particularly of the liver and CNS, expression of this gene at significantly higher or lower levels may be routinely detected in certain tissues or cell types (e.g. liver, cancerous and wounded tissues) or bodily fluids (e.g. lymph, serum, plasma, urine, synovial fluid and spinal fluid) or another tissue or cell sample taken from an individual having such a disorder, relative to the standard gene expression

level, i.e., the expression level in healthy tissue or bodily fluid from an individual not having the disorder.

Predicted epitopes include those comprising a sequence shown in SEQ ID NO: 268 as residues: Gln-26 to Lys-34.

The tissue distribution in fetal liver and neural tissues indicates that the protein product of this gene is useful for the diagnosis and treatment for liver diseases such as hepatocellular carcinomas and diseases of the CNS. Furthermore, the tissue distribution indicates that the protein product of this gene is useful for the detection and treatment of liver disorders and cancers (e.g. hepatoblastoma, jaundice, hepatitis, liver metabolic diseases and conditions that are attributable to the differentiation of hepatocyte progenitor cells), as well as the detection and treatment of neurodegenerative disease states and behavioral disorders such as Alzheimer's Disease, Parkinson's Disease, Huntington's Disease, Tourette's Syndrome, schizophrenia, mania, dementia, paranoia, obsessive compulsive disorder, panic disorder, learning disabilities, ALS, psychoses , autism, and altered behaviors, including disorders in feeding, sleep patterns, balance, and perception.

Many polynucleotide sequences, such as EST sequences, are publicly available and accessible through sequence databases. Some of these sequences are related to SEQ ID NO:30 and may have been publicly available prior to conception of the present invention. Preferably, such related polynucleotides are specifically excluded from the scope of the present invention. To list every related sequence is cumbersome. Accordingly, preferably excluded from the present invention are one or more polynucleotides comprising a nucleotide sequence described by the general formula of a-b, where a is any integer between 1 to 1653 of SEQ ID NO:30, b is an integer of 15 to 1667, where both a and b correspond to the positions of nucleotide residues shown in SEQ ID NO:30, and where b is greater than or equal to a + 14.

FEATURES OF PROTEIN ENCODED BY GENE NO: 21

The translation product of this gene shows sequence homology to two recently cloned genes, karyopherin beta 3 and Ran_GTP binding protein 5. (See Genbank

Accession Nos. gi|2102696 and gnl|PID|e328731.) The Ran_GTP binding protein is related to importin-beta, the key mediator of nuclear localization signal (NLS)-dependent nuclear transport. Based on homology, it is likely that this gene may demonstrate activity similar to the RAN_GTP binding protein.

In specific embodiments, polypeptides of the invention comprise, or alternatively consists of, the following amino acid sequence: VRVAAAESMXLLLECAXVRGPEYLTQMWHFMCDALIKAIGTEPDSDVLSEI MHSFAK (SEQ ID NO:545). Moreover, fragments and variants of this polypeptide (such as, for example, fragments as described herein, polypeptides at least 80%, 85%, 90%, 95%, 96%, 97%, 98%, or 99% identical to these polypeptides and polypeptides encoded by the polynucleotide which hybridize, under stringent conditions, to the polynucleotide encoding this polypeptide are encompassed by the invention. Antibodies that bind polypeptides of the invention are also encompassed by the invention. Polynucleotides encoding this polypeptide are also encompassed by the invention.

This gene is expressed in thymus tissue, and to a lesser extent in stromal cells.

Polynucleotides and polypeptides of the invention are useful as reagents for differential identification of the tissue(s) or cell type(s) present in a biological sample and for diagnosis of diseases and conditions which include, but are not limited to, immune disorders. Similarly, polypeptides and antibodies directed to these polypeptides are useful in providing immunological probes for differential identification of the tissue(s) or cell type(s). For a number of disorders of the above tissues or cells, particularly of the immune system, expression of this gene at significantly higher or lower levels may be routinely detected in certain tissues or cell types (e.g. immune, thymus, cancerous and wounded tissues) or bodily fluids (e.g. lymph, serum, plasma, urine, synovial fluid and spinal fluid) or another tissue or cell sample taken from an individual having such a disorder, relative to the standard gene expression level, i.e., the expression level in healthy tissue or bodily fluid from an individual not having the disorder.

The tissue distribution in thymus indicates that the protein product of this gene is useful for the diagnosis and treatment for immune disorders. Furthermore, the polypeptides or polynucleotides of the present invention are also useful in the

treatment, prophylaxis, and detection of thymus disorders, such as Graves Disease, lymphocytic thyroiditis, hyperthyroidism, and hypothyroidism. Additionally, the tissue distribution indicates that the protein product of this gene is useful for the treatment and diagnosis of hematopoetic related disorders such as anemia, pancytopenia, leukopenia, thrombocytopenia or leukemia, since stromal cells are important in the production of cells of hematopoietic lineages. The uses include bone marrow cell ex vivo culture, bone marrow transplantation, bone marrow reconstitution, radiotherapy or chemotherapy of neoplasia. The gene product may also be involved in lymphopoiesis, therefore, it can be used in immune disorders such as infection, inflammation, allergy, immunodeficiency etc. In addition, this gene product may have commercial utility in the expansion of stem cells and committed progenitors of various blood lineages, and in the differentiation and/or proliferation of various cell types.

Many polynucleotide sequences, such as EST sequences, are publicly available and accessible through sequence databases. Some of these sequences are related to SEQ ID NO:31 and may have been publicly available prior to conception of the present invention. Preferably, such related polynucleotides are specifically excluded from the scope of the present invention. To list every related sequence is cumbersome. Accordingly, preferably excluded from the present invention are one or more polynucleotides comprising a nucleotide sequence described by the general formula of a-b, where a is any integer between 1 to 1394 of SEQ ID NO:31, b is an integer of 15 to 1408, where both a and b correspond to the positions of nucleotide residues shown in SEQ ID NO:31, and where b is greater than or equal to a + 14.

FEATURES OF PROTEIN ENCODED BY GENE NO: 22

The translation product of this gene shares sequence homology with a natural resistance-associated macrophage protein 2 from Homo sapiens (gi|3152690 (AF064484)), which is thought to function as a macrophage-specific membrane transport protein. This gene is expressed primarily in prostate and osteoclastoma tissues. In specific embodiments, polypeptides of the invention comprise, or

alternatively consists of, an amino acid sequence selected from the group: MEINNQNCFIVIDLVRTVMENGVEGLLIFGAFLPESWLIGVRCSSEPPKALLLIL AHSQKRRLDGWSFIRHLRVHYCVSLTIHFS (SEQ ID NO:546), GGREANKXFFIESCIALFVSFIINVFVVSVFAEXFFGXTNEQVVEVCTNTSSPH AGLFPKDNSTLAVDIYKGGVVLGCYFGPAALYIWAVGILAAGQSST (SEQ ID NO:547), GGREANKXFFIESCIALFVSFIINVFVVSVFAEXFFGXTNEQVVE (SEQ ID NO:548), and/or VCTNTSSPHAGLFPKDNSTLAVDIYKGGVVLGCYFGPAALYIWAVGILAAGQ SST (SEQ ID NO:549). Moreover, fragments and variants of these polypeptides (such as, for example, fragments as described herein, polypeptides at least 80%, 85%, 90%, 95%, 96%, 97%, 98%, or 99% identical to these polypeptides and polypeptides encoded by the polynucleotide which hybridizes, under stringent conditions, to the polynucleotide encoding these polypeptides) are encompassed by the invention. Antibodies that bind polypeptides of the invention are also encompassed by the invention. Polynucleotides encoding these polypeptides are also encompassed by the invention.

The gene encoding the disclosed cDNA is thought to reside on chromosome 12. Accordingly, polynucleotides related to this invention are useful as a marker in linkage analysis for chromosome 12.

This gene is expressed primarily in fetal liver/spleen, fetal brain, and to a lesser extent in placenta.

Polynucleotides and polypeptides of the invention are useful as reagents for differential identification of the tissue(s) or cell type(s) present in a biological sample and for diagnosis of diseases and conditions which include, but are not limited to, immune, developmental, hepatic, or bone and prostate diseases, and cancers, particularly of the bone and prostate. Similarly, polypeptides and antibodies directed to these polypeptides are useful in providing immunological probes for differential identification of the tissue(s) or cell type(s). For a number of disorders of the above tissues or cells, particularly of the bone and prostate systems, expression of this gene at significantly higher or lower levels may be routinely detected in certain tissues or cell types (e.g. bone, prostate, cancerous and wounded tissues) or bodily fluids (e.g. lymph, serum, plasma, urine, synovial fluid and spinal fluid) or another tissue or cell

sample taken from an individual having such a disorder, relative to the standard gene expression level, i.e., the expression level in healthy tissue or bodily fluid from an individual not having the disorder.

The tissue distribution in bone indicates that the protein product of this gene is useful for the diagnosis and treatment of bone and prostate disorders, especially cancers of those systems. Elevated levels of expression of this gene product in osteoclastoma indicates that it may play a role in the survival, proliferation, and/or growth of osteoclasts. Therefore, it may be useful in influencing bone mass in such conditions as osteoporosis. Moreover, the protein product of this gene is useful for the treatment and diagnosis of hematopoietic related disorders such as anemia, pancytopenia, leukopenia, thrombocytopenia or leukemia since stromal cells are important in the production of cells of hematopoietic lineages. The uses include bone marrow cell ex vivo culture, bone marrow transplantation, bone marrow reconstitution, radiotherapy or chemotherapy of neoplasia. The gene product may also be involved in lymphopoiesis, therefore, it can be used in immune disorders such as infection, inflammation, allergy, immunodeficiency etc. In addition, this gene product may have commercial utility in the expansion of stem cells and committed progenitors of various blood lineages, and in the differentiation and/or proliferation of various cell types. Protein, as well as, antibodies directed against the protein may show utility as a tumor marker and/or immunotherapy targets for the above listed tissues.

Many polynucleotide sequences, such as EST sequences, are publicly available and accessible through sequence databases. Some of these sequences are related to SEQ ID NO:32 and may have been publicly available prior to conception of the present invention. Preferably, such related polynucleotides are specifically excluded from the scope of the present invention. To list every related sequence is cumbersome. Accordingly, preferably excluded from the present invention are one or more polynucleotides comprising a nucleotide sequence described by the general formula of a-b, where a is any integer between 1 to 3172 of SEQ ID NO:32, b is an integer of 15 to 3186, where both a and b correspond to the positions of nucleotide residues shown in SEQ ID NO:32, and where b is greater than or equal to a + 14.

FEATURES OF PROTEIN ENCODED BY GENE NO: 23

This gene shares sequence homology with the FK506-binding protein (FKBP-13) family, a known cytosolic receptor for the immunosuppressants FK506 and rapamycin. Recently, another group has cloned a very similar gene, recognizing the homology to the FK506-binding protein family, calling their gene FKBP23 (See Genbank Accession No. 2827255.). Contact of cells with supernatant expressing the product of this gene increases the permeability of both prostate stromal cells and dermal fibroblasts to calcium. Thus, it is likely that the product of this gene is involved in a signal transduction pathway that is initiated when the product of this gene binds receptors on the surface of stromal cells and dermal fibroblast cells. Thus, polynucleotides and polypeptides have uses which include, but are not limited to, activating stromal and fibroblast cells.

This gene is expressed primarily in lymphoid tissues and stromal cells.

Polynucleotides and polypeptides of the invention are useful as reagents for differential identification of the tissue(s) or cell type(s) present in a biological sample, especially for those susceptible to immune suppressant therapies and for diagnosis of diseases and conditions which include, but are not limited to, immune suppressant disorders. Similarly, polypeptides and antibodies directed to these polypeptides are useful in providing immunological probes for differential identification of the tissue(s) or cell type(s). For a number of disorders of the above tissues or cells, particularly of the immune system, expression of this gene at significantly higher or lower levels may be routinely detected in certain tissues or cell types (e.g. immune, cancerous and wounded tissues) or bodily fluids (e.g. lymph, serum, plasma, urine, synovial fluid and spinal fluid) or another tissue or cell sample taken from an individual having such a disorder, relative to the standard gene expression level, i.e., the expression level in healthy tissue or bodily fluid from an individual not having the disorder.

Predicted epitopes include those comprising a sequence shown in SEQ ID NO: 271 as residues: Ala-19 to Val-31, Arg-38 to Gly-49, Ala-61 to Lys-66, Tyr-68

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to Pro-78, Gly-116 to Ala-121, Asp-154 to Ser-162, Glu-173 to Gln-186, Phe-194 to Gly-203, and/or Pro-207 to Val-212.

The tissue distribution in lymphoid tissues and stromal cells, the biological activity data, combined with the homology to FKBP-12 and -13 indicates that the protein product of this gene is useful for the diagnosis and treatment of immune suppressant disorders.

Many polynucleotide sequences, such as EST sequences, are publicly available and accessible through sequence databases. Some of these sequences are related to SEQ ID NO:33 and may have been publicly available prior to conception of the present invention. Preferably, such related polynucleotides are specifically excluded from the scope of the present invention. To list every related sequence is cumbersome. Accordingly, preferably excluded from the present invention are one or more polynucleotides comprising a nucleotide sequence described by the general formula of a-b, where a is any integer between 1 to 957 of SEQ ID NO:33, b is an integer of 15 to 971, where both a and b correspond to the positions of nucleotide residues shown in SEQ ID NO:33, and where b is greater than or equal to a + 14.

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FEATURES OF PROTEIN ENCODED BY GENE NO: 24

The gene encoding the disclosed cDNA is thought to reside on chromosome 8. Accordingly, polynucleotides related to this invention are useful as a marker in linkage analysis for chromosome 8.

This gene is expressed primarily in the brain and in the retina.

Polynucleotides and polypeptides of the invention are useful as reagents for differential identification of the tissue(s) or cell type(s) present in a biological sample and for diagnosis of diseases and conditions which include, but are not limited to, neurological and ocular associated disease states. Similarly, polypeptides and antibodies directed to these polypeptides are useful in providing immunological probes for differential identification of the tissue(s) or cell type(s). For a number of disorders of the above tissues or cells, particularly of the disorders of the central nervous system, expression of this gene at significantly higher or lower levels may be

routinely detected in certain tissues or cell types (e.g. brain, cancerous and wounded tissues) or bodily fluids (e.g. lymph, serum, plasma, urine, synovial fluid and spinal fluid) or another tissue or cell sample taken from an individual having such a disorder, relative to the standard gene expression level, i.e., the expression level in healthy tissue or bodily fluid from an individual not having the disorder.

Predicted epitopes include those comprising a sequence shown in SEQ ID NO: 272 as residues: Cys-34 to Asp-40.

The tissue distribution in retina indicates that the protein product of this gene is useful for the treatment and/or detection of eye disorders including blindness, color blindness, impaired vision, short and long sightedness, retinitis pigmentosa, retinitis proliferans, and retinoblastoma. Expression in the brain indicates a role in the is useful for the detection/treatment of neurodegenerative disease states and behavioral disorders such as Alzheimer's Disease, Parkinson's Disease, Huntington's Disease, schizophrenia, mania, dementia, paranoia, obsessive compulsive disorder and panic disorder.

Many polynucleotide sequences, such as EST sequences, are publicly available and accessible through sequence databases. Some of these sequences are related to SEQ ID NO:34 and may have been publicly available prior to conception of the present invention. Preferably, such related polynucleotides are specifically excluded from the scope of the present invention. To list every related sequence is cumbersome. Accordingly, preferably excluded from the present invention are one or more polynucleotides comprising a nucleotide sequence described by the general formula of a-b, where a is any integer between 1 to 1778 of SEQ ID NO:34, b is an integer of 15 to 1792, where both a and b correspond to the positions of nucleotide residues shown in SEQ ID NO:34, and where b is greater than or equal to a + 14.

FEATURES OF PROTEIN ENCODED BY GENE NO: 25

This gene shows sequence homology to a newly identified class of proteins expressed in the nervous system, called stathmin family. (See Genbank Accession No. 2585991; see also Eur. J. Biochem. 248 (3), 794-806 (1997).) The stathmin

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family appears to be an ubiquitous phosphoprotein involved as a relay integrating various intracellular signaling pathways. These pathways affect cell proliferation and differentiation.

In specific embodiments, polypeptides of the invention comprise, or alternatively consists of, an amino acid sequence selected from the group: QDKHAEEVRKNKELKEEASR (SEQ ID NO:550), QQDLSPWAAPVGCPLXXASXTCHXLPLSGCLRRQSXSLPVVAXLCFWFSCPL ASLFVPGQPCVTCPFPSLPFQDKHAEEVRKNKELKEEASR (SEQ ID NO:551). Moreover, fragments and variants of these polypeptides (such as, for example, fragments as described herein, polypeptides at least 80%, 85%, 90%, 95%, 96%, 97%, 98%, or 99% identical to these polypeptides and polypeptides encoded by the polynucleotide which hybridizes, under stringent conditions, to the polynucleotide encoding these polypeptides) are encompassed by the invention. Antibodies that bind polypeptides of the invention are also encompassed by the invention. Polynucleotides encoding these polypeptides are also encompassed by the invention.

This gene is expressed highly in brain tissues.

Polynucleotides and polypeptides of the invention are useful as reagents for differential identification of the tissue(s) or cell type(s) present in a biological sample and for diagnosis of diseases and conditions which include, but are not limited to, neurological disorders. Similarly, polypeptides and antibodies directed to these polypeptides are useful in providing immunological probes for differential identification of the tissue(s) or cell type(s). For a number of disorders of the above tissues or cells, particularly of the central nervous system, expression of this gene at significantly higher or lower levels may be routinely detected in certain tissues or cell types (e.g. brain, cancerous and wounded tissues) or bodily fluids (e.g. lymph, serum, plasma, urine, synovial fluid and spinal fluid) or another tissue or cell sample taken from an individual having such a disorder, relative to the standard gene expression level, i.e., the expression level in healthy tissue or bodily fluid from an individual not having the disorder.

The tissue distribution in brain indicates that the protein product of this gene is useful for the detection/treatment of neurodegenerative disease states and behavioral disorders such as Alzheimer's Disease, Parkinson's Disease, Huntington's Disease,

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schizophrenia, mania, dementia, paranoia, obsessive compulsive disorder and panic disorder.

Many polynucleotide sequences, such as EST sequences, are publicly available and accessible through sequence databases. Some of these sequences are related to SEQ ID NO:35 and may have been publicly available prior to conception of the present invention. Preferably, such related polynucleotides are specifically excluded from the scope of the present invention. To list every related sequence is cumbersome. Accordingly, preferably excluded from the present invention are one or more polynucleotides comprising a nucleotide sequence described by the general formula of a-b, where a is any integer between 1 to 882 of SEQ ID NO:35, b is an integer of 15 to 896, where both a and b correspond to the positions of nucleotide residues shown in SEQ ID NO:35, and where b is greater than or equal to a + 14.

FEATURES OF PROTEIN ENCODED BY GENE NO: 26

The polynucleotide sequence of this gene contains a domain similar to a Flt3 ligand peptide.

In specific embodiments, polypeptides of the invention comprise, or alternatively consists of, the following amino acid sequence: PTRCCTTQPCRSSARRPCWVPMVPSPEGREXQPTCPS (SEQ ID NO:552). Moreover, fragments and variants of this polypeptide (such as, for example, fragments as described herein, polypeptides at least 80%, 85%, 90%, 95%, 96%, 97%, 98%, or 99% identical to these polypeptides and polypeptides encoded by the polynucleotide which hybridize, under stringent conditions, to the polynucleotide encoding this polypeptide are encompassed by the invention. Antibodies that bind polypeptides of the invention are also encompassed by the invention. Polynucleotides encoding this polypeptide are also encompassed by the invention.

This gene may have activity as binding to Flt3 receptors, a process known to promote angiogenesis and/or lymphangiogenesis.

This gene is expressed in human tonsil, and to a lesser extent in teratocarcinoma, placenta, colon carcinoma, and fetal kidney.

Therefore, polynucleotides and polypeptides of the invention are useful as reagents for identification of the tissue(s) or cell type(s) present in a biological sample and for diagnosis of diseases and conditions which include, but are not limited to, diseases of the tonsil, as well as cancers, such as colon, reproductive, and kidney cancers. Similarly, polypeptides and antibodies directed to these polypeptides are useful in providing immunological probes for differential identification of the tissue(s) or cell type(s). For a number of disorders of the above tissues or cells, particularly of the tonsils, colon, reproductive organs, and kidneys, expression of this gene at significantly higher or lower levels may be routinely detected in certain tissues or cell types (e.g. immune, tonsils, colon, kidney, cancerous and wounded tissues) or bodily fluids (e.g. lymph, serum, plasma, urine, synovial fluid and spinal fluid) or another tissue or cell sample taken from an individual having such a disorder, relative to the standard gene expression level, i.e., the expression level in healthy tissue or bodily fluid from an individual not having the disorder.

Predicted epitopes include those comprising a sequence shown in SEQ ID NO: 274 as residues: Pro-22 to Glu-33.

The tissue distribution in tonsils, several cancers, and fetal tissues indicates that the protein product of this gene is useful for the diagnosis and treatment of diseases of the tonsil or colon, such as tonsilitis, inflammatory diseases involving nose and paranasal sinuses, especially during the infection of influenza, adenoviruses, parainfluenza, or rhinoviruses, for example. The gene may also be useful in the diagnosis and treatment of neoplasms of nasopharynx or colon origins. Protein, as well as, antibodies directed against the protein may show utility as a tumor marker and/or immunotherapy targets for the above listed tissues.

Many polynucleotide sequences, such as EST sequences, are publicly available and accessible through sequence databases. Some of these sequences are related to SEQ ID NO:36 and may have been publicly available prior to conception of the present invention. Preferably, such related polynucleotides are specifically excluded from the scope of the present invention. To list every related sequence is cumbersome. Accordingly, preferably excluded from the present invention are one or more polynucleotides comprising a nucleotide sequence described by the general formula of a-b, where a is any integer between 1 to 898 of SEQ ID NO:36, b is an

integer of 15 to 912, where both a and b correspond to the positions of nucleotide residues shown in SEQ ID NO:36, and where b is greater than or equal to a + 14.

FEATURES OF PROTEIN ENCODED BY GENE NO: 27

In specific embodiments, polypeptides of the invention comprise, or alternatively consists of, an amino acid sequence selected from the group: MKRSLNENSARSTAGCLPVPLFNQKKRNRQPLTSNPLKDDSGISTPSDNYDFP PLPTDWAWEAVNPEXAPVMKTVDTGQIPHSVSRPLRSQDSVFNSIQSNTGRS QGGWSYRDGNKNTSLKTWXKNDFKPQCKRTNLVANDGKNSCPMSSGAQQ QKQLRTPEPPNLSRNKETELLRQTHSSKISGCTMRGLDKNSALQTLKPNFQQN QYKXQMLDDIPEDNTLKETSLYQLQFKEKASSLRIISAVIESMKYWREHAQKT VLLFEVLAVLDSAVTPGPYYSKTFLMRDGKNTLPCVFYEIDRELPRLIRGRVH RCVGNYDQKKNIFQCVSVRPASVSEQKTFQAFVKIADVEMQYYINVMNET (SEQ ID NO:553), SQDSVFNSIQSNTGRSQGGWSYRDGNKNTSLKTWXKNDFKPQCKR (SEQ ID NO:554), NKETELLRQTHSSKISGCTMRGLDKNSALQTLKPNF (SEQ ID NO:555), SSLRIISAVIESMKYWREHAQKTVLLFEVLAVLDSAVTPGPYYSKTFLM (SEQ ID NO:556), and/or PRLIRGRVHRCVGNYDQKKNIFQCVSVRPASVSEQKTFQAFV (SEQ ID NO:557). Moreover, fragments and variants of these polypeptides (such as, for example, fragments as described herein, polypeptides at least 80%, 85%, 90%, 95%, 96%, 97%, 98%, or 99% identical to these polypeptides and polypeptides encoded by the polynucleotide which hybridizes, under stringent conditions, to the polynucleotide encoding these polypeptides) are encompassed by the invention. Antibodies that bind polypeptides of the invention are also encompassed by the invention. Polynucleotides encoding these polypeptides are also encompassed by the invention.

This gene is expressed primarily in human testes.

Polynucleotides and polypeptides of the invention are useful as reagents for differential identification of the tissue(s) or cell type(s) present in a biological sample

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and for diagnosis of diseases and conditions which include, but are not limited to, male reproductive disorders, including cancer. Similarly, polypeptides and antibodies directed to these polypeptides are useful in providing immunological probes for differential identification of the tissue(s) or cell type(s). For a number of disorders of the above tissues or cells, particularly of the male reproductive system, expression of this gene at significantly higher or lower levels may be routinely detected in certain tissues or cell types (e.g. testes, cancerous and wounded tissues) or bodily fluids (e.g. lymph, serum, seminal fluid, plasma, urine, synovial fluid and spinal fluid) or another tissue or cell sample taken from an individual having such a disorder, relative to the standard gene expression level, i.e., the expression level in healthy tissue or bodily fluid from an individual not having the disorder.

The tissue distribution in human testes indicates that the protein product of this gene is useful as a hormone with reproductive or other systemic functions; contraceptive development; male infertility of testicular causes, such as Kleinfelter's syndrome, varicocele, orchitis; male sexual dysfunctions; testicular neoplasms; and inflammatory disorders such as epididymitis. Furthermore, this gene product is useful in the treatment of male infertility and/or impotence. This gene product is also useful in assays designed to identify binding agents as such agents (antagonists) are useful as male contraceptive agents. Similarly, the protein is believed to by useful in the treatment and/or diagnosis of testicular cancer. The testes are also a site of active gene expression of transcripts that may be expressed, particularly at low levels, in other tissues of the body. Therefore, this gene product may be expressed in other specific tissues or organs where it may play related functional roles in other processes, such as hematopoiesis, inflammation, bone formation, and kidney function, to name a few possible target indications.

Many polynucleotide sequences, such as EST sequences, are publicly available and accessible through sequence databases. Some of these sequences are related to SEQ ID NO:37 and may have been publicly available prior to conception of the present invention. Preferably, such related polynucleotides are specifically excluded from the scope of the present invention. To list every related sequence is cumbersome. Accordingly, preferably excluded from the present invention are one or more polynucleotides comprising a nucleotide sequence described by the general

formula of a-b, where a is any integer between 1 to 1368 of SEQ ID NO:37, b is an integer of 15 to 1382, where both a and b correspond to the positions of nucleotide residues shown in SEQ ID NO:37, and where b is greater than or equal to a + 14.

FEATURES OF PROTEIN ENCODED BY GENE NO: 28

This gene is expressed primarily in apoptotic T-cell.

Polynucleotides and polypeptides of the invention are useful as reagents for differential identification of the tissue(s) or cell type(s) present in a biological sample and for diagnosis of diseases and conditions which include, but are not limited to, diseases relating to T cells, as well as cancer in general. Similarly, polypeptides and antibodies directed to these polypeptides are useful in providing immunological probes for differential identification of the tissue(s) or cell type(s). For a number of disorders of the above tissues or cells, particularly of the disorders of the immune system, expression of this gene at significantly higher or lower levels may be routinely detected in certain tissues or cell types (e.g. immune, cancerous and wounded tissues) or bodily fluids (e.g. lymph, serum, plasma, urine, synovial fluid and spinal fluid) or another tissue or cell sample taken from an individual having such a disorder, relative to the standard gene expression level, i.e., the expression level in healthy tissue or bodily fluid from an individual not having the disorder.

The tissue distribution in apoptotic T-cells indicates that the protein product of this gene is useful for the detection and/or treatment of disorders of the immune system. Moreover, since the gene was isolated from an apoptotic cell, and based on the understanding of the relationship of apoptosis and cancer, it is likely that this gene may play a role in the genesis of cancer. Furthermore, expression of this gene product in T cells also strongly indicates a role for this protein in immune function and immune surveillance.

Many polynucleotide sequences, such as EST sequences, are publicly available and accessible through sequence databases. Some of these sequences are related to SEQ ID NO:38 and may have been publicly available prior to conception of the present invention. Preferably, such related polynucleotides are specifically

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excluded from the scope of the present invention. To list every related sequence is cumbersome. Accordingly, preferably excluded from the present invention are one or more polynucleotides comprising a nucleotide sequence described by the general formula of a-b, where a is any integer between 1 to 858 of SEQ ID NO:38, b is an integer of 15 to 872, where both a and b correspond to the positions of nucleotide residues shown in SEQ ID NO:38, and where b is greater than or equal to a + 14.

FEATURES OF PROTEIN ENCODED BY GENE NO: 29

This gene is expressed primarily in human tonsils.

Polynucleotides and polypeptides of the invention are useful as reagents for differential identification of the tissue(s) or cell type(s) present in a biological sample and for diagnosis of diseases and conditions which include, but are not limited to, gastrointestinal and immune disorders. Similarly, polypeptides and antibodies directed to these polypeptides are useful in providing immunological probes for differential identification of the tissue(s) or cell type(s). For a number of disorders of the above tissues or cells, particularly of the gastrointestinal and immune system, expression of this gene at significantly higher or lower levels may be routinely detected in certain tissues or cell types (e.g. immune, gastrointestinal, cancerous and wounded tissues) or bodily fluids (e.g. lymph, serum, plasma, urine, synovial fluid and spinal fluid) or another tissue or cell sample taken from an individual having such a disorder, relative to the standard gene expression level, i.e., the expression level in healthy tissue or bodily fluid from an individual not having the disorder.

The tissue distribution in human tonsils indicates that the protein product of this gene is useful for the diagnosis and treatment of gastrointestinal diseases. Alternatively, the tissue distribution indicates that the protein product of this gene is useful for the diagnosis and treatment of a variety of immune system disorders. Expression of this gene product in tonsils indicates a role in the regulation of the proliferation; survival; differentiation; and/or activation of potentially all hematopoietic cell lineages, including blood stem cells. This gene product may be involved in the regulation of cytokine production, antigen presentation, or other

processes that may also suggest a usefulness in the treatment of cancer (e.g. by boosting immune responses). Since the gene is expressed in cells of lymphoid origin, the gene or protein, as well as, antibodies directed against the protein may show utility as a tumor marker and/or immunotherapy targets for the above listed tissues. Therefore it may be also used as an agent for immunological disorders including arthritis, asthma, immune deficiency diseases such as AIDS, leukemia, rheumatoid arthritis, inflammatory bowel disease, sepsis, acne, and psoriasis. In addition, this gene product may have commercial utility in the expansion of stem cells and committed progenitors of various blood lineages, and in the differentiation and/or proliferation of various cell types. Protein, as well as, antibodies directed against the protein may show utility as a tumor marker and/or immunotherapy targets for the above listed tissues.

Many polynucleotide sequences, such as EST sequences, are publicly available and accessible through sequence databases. Some of these sequences are related to SEQ ID NO:39 and may have been publicly available prior to conception of the present invention. Preferably, such related polynucleotides are specifically excluded from the scope of the present invention. To list every related sequence is cumbersome. Accordingly, preferably excluded from the present invention are one or more polynucleotides comprising a nucleotide sequence described by the general formula of a-b, where a is any integer between 1 to 798 of SEQ ID NO:39, b is an integer of 15 to 812, where both a and b correspond to the positions of nucleotide residues shown in SEQ ID NO:39, and where b is greater than or equal to a + 14.

FEATURES OF PROTEIN ENCODED BY GENE NO:30

This gene is expressed primarily in human T-cells, and to a lesser extent, in human colon carcinoma.

The translation product of this gene shares sequence homology with C44C1.2 gene product of Caenorhabditis elegans.

Preferred polypeptides of the present invention comprise, or alternatively consist of, one, two, three, four, five, six, seven or all seven of the immunogenic epitopes shown in SEQ ID NO:278 as residues: Leu-21 to Ala-30, Ser-38 to Asp-47, Pro-87 to Asp-94, Leu-197 to Thr-204, Pro-256 to Ser-262, Thr-277 to Arg-282,

and/or Thr-293 to Trp-303. Polynucleotides encoding these polypeptides are also encompassed by the invention, as are antibodies that bind one or more of these peptides.

Additionally, preferred polypeptides of the present invention comprise, or alternatively consist of, one, two, or both of the immunogenic epitopes shown in SEQ ID NO:1232 as residues: Gly-204 to Gly-234 and Arg-202 to Asp-236. Polynucleotides encoding these polypeptides are also encompassed by the invention, as are antibodies that bind one or more of these polypeptides.

In additional nonexclusive embodiments, preferred polypeptides of the invention also comprise, or alternatively consist of, one or more of the following amino acid sequences: Gly-188 to Val-203, Gly-188 to Thr-204, Thr-204 to Lys-257, Asp-280 to Leu-362 of SEQ ID 278 and Gly-204 to Gly-234 of SEQ ID NO: 1232. Polynucleotides encoding these polypeptides are also encompassed by the invention, as are antibodies that bind one or more of these peptides.

In specific embodiments, polypeptides of the invention comprise, or alternatively consists of, an amino acid sequence selected from the group:
GVFRPCVCGRPASLTCSPLDPEVGPYCDTPTMRTLFNLLWLALACSPVHTTLS
KSDAKKAASKTLLEKSQFSDKPVQDRGLVVTDLKAESVVLEHRSYCSAKAR
DRHFAGDVLGYVTPWNSHGYDVTKVFGSKFTQISPVWLQLKRRGREMFEVT
GLHDVDQGWMRAVRKHAKGLHIVPRLLFEDWTYDDFRNVLDSEDEIEELSK
TVVQVAKNQHFDGFVVEVWNQLLSQKRVGLIHMLTHLAEALHQARLLALL
VIPPAITPGTDQLGMFTHKEFEQLAPVLDGFSLMTYDYSTAHQPGPNAPLSWV
RACVQVLDPKXKWRTKSSWGSTSMXWTXRXPXDARXPVVGXRXIQXLKDH
XPRMVLDSKPQ (SEQ ID NO:558),
TCSPLDPEVGPYCDTPTMRTLFNLLWLALACSPVHTTLS (SEQ ID NO:559),
LVVTDLKAESVVLEHRSYCSAKARDRHFAGDVLGYVTPWNSHGYDVTKVF
GSKF (SEQ ID NO:560),
REMFEVTGLHDVDQGWMRAVRKHAKGLHIVPRLLFEDWTYDDFRNVLDSE
DE (SEQ ID NO:561),
HFDGFVVEVWNQLLSQKRVGLIHMLTHLAEALHQARLLALLVIPPAITPGTD
QLGM (SEQ ID NO:562), and
DGFSLMTYDYSTAHQPGPNAPLSWVRACVQVLDPKXKWRTKSSWGST (SEQ

ID NO:563). Moreover, fragments and variants of these polypeptides (such as, for example, fragments as described herein, polypeptides at least 80%, 85%, 90%, 95%, 96%, 97%, 98%, or 99% identical to these polypeptides and polypeptides encoded by the polynucleotide which hybridizes, under stringent conditions, to the polynucleotide encoding these polypeptides) are encompassed by the invention. Antibodies that bind polypeptides of the invention are also encompassed by the invention. Polynucleotides encoding these polypeptides are also encompassed by the invention.

In additional nonexclusive embodiments, polynucleotides of the invention comprise or alternatively consist of, one or more of the following sequences:

GGCACGAGCGTTTTCCGGCCGTGCGTTTGTGGCCGTCCGGCCTCCC
TGACATGCAGCCCTCTGGACCCCGAGGTTGGACCCTACTGTGACACACCT
ACCATGCGGACACTCTTCAACCTCCTCTGGCTTGCCCTGGCCTGCAGCCCT
GTTCACACTACCCTGTCAAAGTCAGATGCCAAAAAAGCCGCCTCAAAGAC
GCTGCTGGAGAAGAGTCAGTTTTCAGATAAGCCGGTGCAAGACCGGGGTT
TGGTGGTGACGGACCTCAAAGCTGAGAGTGTGGTTCTTGAGCATCGCAGC
TACTGCTCGGCAAAGGCCCGGGACAGACACTTTGCTGGGGATGTACTGGG
CTATGTCACTCCATGGAACAGCCATGGCTACGATGTCACCAAGGTCTTTG
GGAGCAAGTTCACACAGATCTCACCCGTCTGGCTGCAGCTGAAGAGACGT
GGCCGTGAGATGTTTGAGGTCACGGGCCTCCACGACGTGGACCAAGGGTG
GATGCGAGCTGTCAGGAAGCATGCCAAGGGCCTGCACATAGTGCCTCGGC
TCCTGTTTGAGGACTGGACTTACGATGATTTCCGGAACGTCTTAGACAGTG
AGGATGAGATAGAGGAGCTGAGCAAGACCGTGGTCCAGGTGGCAAAGAA
CCAGCATTTCGATGGCTTCGTGGTGGAGGTCTGGAACCAGCTGCTAAGCC
AGAAGCGCGTGGGCCTCATCCACATGCTCACCCACTTGGCCGAGGCTCTG
CACCAGGCCCGGCTGCTGGCCCTCCTGGTCATCCCGCCTGCCATCACCCCC
GGGACCGACCAGCTGGGCATGTTCACGCACAAGGAGTTTGAGCAGCTGGC
CCCCGTGCTGGATGGTTTCAGCCTCATGACCTACGACTACTCTACAGCGCA
TCAGCCTGGCCCTAATGCACCCCTGTCCTGGGTTCGAGCCTGCGTCCAGGT
CCTGGACCCGAAGTCCAAGTGGCGAAGCAAAATCCTCCTGGGGCTCAACT
TCTATGGTACATCCAGACACTGAAGGACCACAGGCCCCGGATGGTGTGGG
ACAGCCAGGTCTCAGAGCACTTCTTCGAGTACAAGAAGAGCCGCAGTGGG
AGGCACGTCGTCTTCTACCCAACCCTGAAGTCCCTGCAGGTGCGGCTGGA

GCTGGCCCGGGAGCTGGGCGTTGGGGTCTCTATCTGGGAGCTGGGCCAGG
GCCTGGACTACTTCTACGACCTGCTCTAGGTGGGCATTGCGGCCTCCGCGG
TGGACGTGTTCTTTTCTAAGCCATGGAGTGAGTGAGCAGGTGTGAAATAC
AGGCCTCCACTCCGAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAA
AAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAAA (SEQ ID NO:1228),
GCGCTGGAGCGTTTTCCGGCCGTGCGTTTGTGGCCGTCCGGCCTCCCTGAC
ATGCAGCCCTCTGGACCCCGAGGTTGGACCCTACTGTGACACACCTACCA
TGCGGACACTCTTCAACCTCCTCTGGCTTGCCCTGGCCTGCAGCCCTGTTC
ACACTACCCTGTCAAAGTCAGATGCCAAAAAAGCCGCCTCAAAGACGCTG
CTGGAGAAGAGTCAGTTTTCAGATAAGCCGGTGCAAGACCGGGGTTTGGT
GGTGACGGACCTCAAAGCTGAGAGTGTGGTTCTTGAGCATCGCAGCTACT
GCTCGGCAAAGGCCCGGGACAGACACTTTGCTGGGGATGTACTGGGCTAT
GTCACTCCATGGAACAGCCATGGCTACGATGTCACCAAGGTCTTTGGGAG
CAAGTTCACACAGATCTCACCCGTCTGGCTGCAGCTGAAGAGACGTGGCC
GTGAGATGTTTGAGGTCACGGGCCTCCACGACGTGGACCAAGGGTGGATG
CGAGCTGTCAGGAAGCATGCCAAGGGCCTGCACATAGTGCCTCGGCTCCT
GTTTGAGGACTGGACTTACGATGATTTCCGGAACGTCTTAGACAGTGAGG
ATGAGATAGAGGAGCTGAGCAAGACCGTGGTCCAGGTGGCAAAGAACCA
GCATTTCGATGGCTTCGTGGTGGAGGTCTGGAACCAGCTGCTAAGCCAGA
AGCGCGTGACCGACCAGCTGGGCATGTTCACGCACAAGGAGTTTGAGCAG
CTGGCCCCCGTGCTGGATGGTTTCAGCCTCATGACCTACGACTACTCTACA
GCGCATCAGCCTGGCCCTAATGCACCCCTGTCCTGGGTTCGAGCCTGCGTC
CAGGTCCTGGACCCGAAGTCCAAGTGGCGAAGCAAAATCCTCCTGGGGCT
CAACTTCTATGGTATGGACTACGCGACCTCCAAGGATGCCCGTGAGCCTG
TTGTCGGGGCCAGGTACATCCAGACACTGAAGGACCACAGGCCCCGGATG
GTGTGGGACAGCCAGGYCTCAGAGCACTTCTTCGAGTACAAGAAGAGCCG
CAGTGGGAGGCACGTCGTCTTCTACCCAACCCTGAAGTCCCTGCAGGTGC
GGCTGGAGCTGGCCCGGGAGCTGGGCGTTGGGGTCTCTATCTGGGAGCTG
GGCCAGGGCCTGGACTACTTCTACGACCTGCTCTAGGTGGGCATTGCGGC
CTCCGCGGTGGACGTGTTCTTTTCTAAGCCATGGAGTGAGTGAGCAGGTG
TGAAATACAGGCCTNCACTCCGTTCAAAAAAAAAAAAAAAAAAAAAAAAA
AAAAAAAAAAAAAAAAAAAAAAAAAACTCGAG (SEQ ID NO: 1229),

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GGCGTTTTCCGGCCGTGCGTTTGTGGCCGTCCGGCCTCCCTGACATGCAGC
CCTCTGGACCCCGAGGTTGGACCCTACTGTGACACACCTACCATGCGGAC
ACTCTTCAACCTCCTCTGGCTTGCCCTGGCCTGCAGCCCTGTTCACACTAC
CCTGTCAAAGTCAGATGCCAAAAAAGCCGCCTCAAAGACGCTGCTGGAGA
AGAGTCAGTTTTCAGATAAGCCGGTGCAAGACCGGGGTTTGGTGGTGACG
GACCTCAAAGCTGAGAGTGTGGTTCTTGAGCATCGCAGCTaCTGCTcGGCA
AAGGCCCGGGACAGACACTTTGCTGGGGATGTACTGGGCTATGTCACTCC
ATGGAACAGCCATGGCTACGATGTCACCAAGGTCTTTGGGAGCAAGTTCA
CACAGATCTCACCCGTCTGGCTGCAGCTGAAGAGACGTGGCCGTGAGATG
TTTGAGGTCACGGGCCTCCACGACGTGGACCAAGGGTGGATGCGAGCTGT
CAGGAAGCATGCCAAGGGCCTGCACATAGTGCCTCGGCTCCTGTTTGAGG
ACTGGACTTACGATGATTTCCGGAACGTCTTAGACAGTGAGGATGAGATA
GAGGAGCTGAGCAAGACCGTGGTCCAGGTGGCAAAGAACCAGCATTTCG
ATGGCTTCGTGGTGGAGGTCTGGAACCAGCTGCTAAGCCAGAAGCGCGTG
GGCCTCATCCACATGCTCACCCACTTGGCCGAGGCTCTGCACCAGGCCCG
GCTGCTGGCCCTCCTGGTCATCCCGCCTGCCATCACCCCCGGGACCGACC
AGCTGGGCATGTTCACGCACAAGGAGTTTGAGCAGCTGGCCCCCGTGCTG
GATGGTTTCAGCCTCATGACCTACGACTACTCTACAGCGCATCAGCCTGGc
CCTAATGCACCCcTGTCCTGGGTTCGAGCCTGCGTCCAGGTCCTGGACCCG
AARTYCAAGTGGCGAACAAAATCCTCCTGGGGSTCAACTTCTATGGWATG
GACTAMGCGACYTCCAANGGATGCCCGTKARCCTGTTGTCGGGGSCAGGT
AMATYCAGAMACTGAARGACCACANGCCCCGGATGGTGTTGGACAGCAA
GCCTCAAAG (SEQ ID NO:1230), and
ATAAGAGACAGCGTCAGGGGGGCGGAGCCTATGGAAAAACGCCAGCAAC
GCGGNCTTTTTACGGTTCCTGGCCTTTTGCTGGCCTTTTGCTCACATGTTCT
TTCCTGCGTTATCCCCTGATTCTGTGGATAACCGTATTACCGCCTTTGAGT
GAGCTGATACCGCTCGCCGCAGCCGAACGACCGAGCGCAGCGAGTCAGT
GAGCGAGGAAGCGGAAGAGCGCCCAATACGCAAACCGCCTCTCCCCGCG
CGTTGGCCGATTCATTAATGCAGCTGGCACGACAGGTTTCCCGACTGGAA
AGCGGGCAGTGAGCGCAACGCAATTAATGTGAGTTAGCTCACTCATTAGG
CACCCCAGGCTTTACACTTTATGCTTCCGGCTCGTATGTTGTGTGGAATTG
TGAGCGGATAACAATTTCACACAGGAAACAGCTATGACCATGATTACGCC

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AAGCTCGAAATTAACCCTCACTAAAGGGAACAAAAGCTGGAGCTCCACCG
CGGTGGCGGCCGCTCTAGAACTAGTGGATCCCCCGGGCTGCAGGAATTCG
GCACGAGGTCCGGCCTCCCTGACATGCAGATTTCCACCCAGAAGACAGAG
AAGGAGCCAGTGGTCATGGAATGGGCTGGGGTCAAAGACTGGGTGCCTG
GGAGCTGAGGCAGCCACCGTTTCAGCCTGGCCAGCCCTCTGGACCCCGAG
GTTGGACCCTACTGTGACACACCTACCATGCGGACACTCTTCAACCTCCTC
TGGCTTGCCCTGGCCTGCAGCCCTGTTCACACTACCCTGTCAAAGTCAGAT
GCCAAAAAAGCCGCCTCAAAGACGCTGCTGGAGAAGAGTCAGTTTTCAGA
TAAGCCGGTGCAAGACCGGGGTTTGGTGGTGACGGACCTCAAAGCTGAGA
GTGTGGTTCTTGAGCATCGCAGCTACTGCTCGGCAAAGGCCCGGGACAGA
CACTTTGCTGGGGATGTACTGGGCTATGTCACTCCATGGAACAGCCATGG
CTACGATGTCACCAAGGTCTTTGGGAGCAAGTTCACACAGATCTCACCCG
TCTGGCTGCAGCTGAAGAGACGTGGCCGTGAGATGTTTGAGGTCACGGGC
CTCCACGACGTGGACCAAGGGTGGATGCGAGCTGTCAGGAAGCATGCCA
AGGGCCTGCACATAGTGCCTCGGCTCCTGTTTGAGGACTGGACTTACGAT
GATTTCCGGAACGTCTTAGACAGTGAGGATGAGATAGAGGAGCTGAGCA
AGACCGTGGTCCAGGTGGCAAAGAACCAGCATTTCGATGGCTTCGTGGTG
GAGGTCTGGAACCAGCTGCTAAGCCAGAAGCGCGTGGGCCTCATCCACAT
GCTCACCCACTTGGCCGAGGCTCTGCACCAGGCCCGGCTGCTGGCCCTCC
TGGTCATCCCGCCTGCCATCACCCCCGGGACCGACCAGCTGGGCATGTTC
ACGCACAAGGAGTTTGAGCAGCTGGCCCCCGTGCTGGATGGTTTCAGCCT
CATGACCTACGACTACTCTACAGCGCATCAGCCTGGCCCTAATGCACCCC
TGTCCTGGGTTCGAGCCTGCGTCCAGGTCCTGGACCCGAAGTCCAAGTGG
CGAAGCAAAATCCTCCTGGGGCTCAACTTCTATGGTACATCCAGACACTG
AAGGACCACAGGCCCCGGATGGTGTGGGACAGCCAGGCCTCAGAGCACT
TCTTCGAGTACAAGAAGAGCCGCAGTGGGAGGCACGTCGTCTTCTACCCA
ACCCTGAAGTCCCTGCAGGTGCGGCTGGAGCTGGCCCGGGAGCTGGGCGT
TGGGGTCTCTATCTGGGAGCTGGGCCAGGGCCTGGACTACTTCTACGACC
TGCTCTAGGTGGGCATTGCGGCCTCCGCGGTGGACGTGTTCTTTTCTAAGC
CATGGAGTGAGTGAGCAGGTGTGAAATACAGGCCTCCACTCCGTTAAAAA
AAAAAAAAAAAAAAAAAACTCGAGGGGGGGCCCGGTACCCAATTCGCCC
TATAGTGAGTCGTATTACAATTCACTGGCCGTCGTTTTACAACGTCGTGAC

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TGGGAAAACCCTGGCGTTACCCAACTTAATCGCCTTGCAGCACATCCCCCT
TTCGCCAGCTGGCGTAATAGCGAAGAGGCCCGCACCGATCGCCCTTCCCA
ACAGTTGCGCAGCCTGAATGGCGAATGGCAAATTGTAAGCGTTAATATTT
TGTTAAAATTCGCGTTAAATTTTTGTTAAATCAGCTCATTTTTTAACCAAT
AGGCCGAAATCGGCAAAATCCCTTATAAATCAAAAGAATAGACCGAGAT
AGGGTTGAGTGTTGNTCCAGTTTGGAACAAGAGTCCACTATTAAAGAACG
TGGACTCCAACGTCAAAGGGCGAAAAACCGNCTATCAGGGCGATGGCCC
ACTACGTGAACCATCACCCTTAATCAAAGTTTTTTGGGGTCGAGGTNCCCC
TAAAAGCACTTAATCGGGAACCC (SEQ ID NO:1231). Polypeptides encoded by these polynucleotides are also encompassed by the invention, as are antibodies that bind to these polypeptides.

In other specific embodiments, polypeptides of the invention comprise, or alternatively consists of, an amino acid sequence selected from the group:
MRTLFNLLWLALACSPVHTTLSKSDAKKAASKTLLEKSQFSDKPVQDRGLVV
TDLKAESVVLEHRSYCSAKARDRHFAGDVLGYVTPWNSHGYDVTKVFGSKF
TQISPVWLQLKRRGREMFEVTGLHDVDQGWMRAVRKHAKGLHIVPRLLFED
WTYDDFRNVLDSEDEIEELSKTVVQVAKNQHFDGFVVEVWNQLLSQKRVGL
IHMLTHLAEALHQARLLALLVIPPAITPGTDQLGMFTHKEFEQLAPVLDGFSL
MTYDYSTAHQPGPNAPLSWVRACVQVLDPKSKWRSKILLGLNFYGTSRH
(SEQ ID NO: 1232),
MRTLFNLLWLALACSPVHTTLSKSDAKKAASKTLLEKSQFSDKPVQDRGLVV
TDLKAESVVLEHRSYCSAKARDRHFAGDVLGYVTPWNSHGYDVTKVFGSKF
TQISPVWLQLKRRGREMFEVTGLHDVDQGWMRAVRKHAKGLHIVPRLLFED
WTYDDFRNVLDSEDEIEELSKTVVQVAKNQHFDGFVVEVWNQLLSQKRVTD
QLGMFTHKEFEQLAPVLDGFSLMTYDYSTAHQPGPNAPLSWVRACVQVLDP
KSKWRSKILLGLNFYGMDYATSKDAREPVVGARYIQTLKDHRPRMVWDSQ
XSEHFFEYKKSRSGRHVVFYPTLKSLQVRLELARELGVGVSIWELGQGLDYF
YDLL (SEQ ID NO: 1233),
MRTLFNLLWLALACSPVHTTLSKSDAKKAASKTLLEKSQFSDKPVQDRGLVV
TDLKAESVVLEHRSYCSAKARDRHFAGDVLGYVTPWNSHGYDVTKVFGSKF
TQISPVWLQLKRRGREMFEVTGLHDVDQGWMRAVRKHAKGLHIVPRLLFED
WTYDDFRNVLDSEDEIEELSKTVVQVAKNQHFDGFVVEVWNQLLSQKRVGL

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IHMLTHLAEALHQARLLALLVIPPAITPGTDQLGMFTHKEFEQLAPVLDGFSL
MTYDYSTAHQPGPNAPLSWVRACVQVLDPKXKWRTKSSWGSTSMXWTXR
XPXDARXPVVGXRX (SEQ ID NO: 1234), and
MRTLFNLLWLALACSPVHTTLSKSDAKKAASKTLLEKSQFSDKPVQDRGLVV
TDLKAESVVLEHRSYCSAKARDRHFAGDVLGYVTPWNSHGYDVTKVFGSKF
TQISPVWLQLKRRGREMFEVTGLHDVDQGWMRAVRKHAKGLHIVPRLLFED
WTYDDFRNVLDSEDEIEELSKTVVQVAKNQHFDGFVVEVWNQLLSQKRVGL
IHMLTHLAEALHQARLLALLVIPPAITPGTDQLGMFTHKEFEQLAPVLDGFSL
MTYDYSTAHQPGPNAPLSWVRACVQVLDPKSKWRSKILLGLNFYGTSRH
(SEQ ID NO: 1235). Moreover, fragments and variants of these polypeptides (such as, for example, fragments as described herein, polypeptides at least 80%, 85%, 90%, 95%, 96%, 97%, 98%, or 99% identical to these polypeptides and polypeptides encoded by the polynucleotide which hybridizes, under stringent conditions, to the polynucleotide encoding these polypeptides) are encompassed by the invention. Antibodies that bind polypeptides of the invention are also encompassed by the invention. Polynucleotides encoding these polypeptides are also encompassed by the invention.

Also preferred are polypeptides, comprising or alternatively consisting of, the mature polypeptide which is predicted to consist of residues 23-362 of the foregoing sequence (SEQ ID NO:278), and biologically active fragments of the mature polypeptide (e.g., fragments that inhibit the Mixed Lymphocyte Reaction). Polynucleotides encoding these polypeptides are also encompassed by the invention

Figures 1A-B show the nucleotide (SEQ ID NO:40) and deduced amino acid sequence (SEQ ID NO: 278) corresponding to this gene.

Figure 2 shows an analysis of the amino acid sequence (SEQ ID NO: 278). Alpha, beta, turn and coil regions; hydrophilicity and hydrophobicity; amphipathic regions; flexible regions; antigenic index and surface probability are shown, and all were generated using the default settings of the recited computer algorithms. In the "Antigenic Index or Jameson-Wolf" graph, the positive peaks indicate locations of the highly antigenic regions of the protein, i.e., regions from which epitope-bearing peptides of the invention can be obtained. Polypeptides comprising, or alternatively

consisting of, domains defined by these graphs are contemplated by the present invention, as are polynucleotides encoding these polypeptides.

The data presented in Figure 2 are also represented in tabular form in Table 3. The columns are labeled with the headings "Res", "Position", and Roman Numerals I-XIV. The column headings refer to the following features of the amino acid sequence presented in Figure 2, and Table 3: "Res": amino acid residue of SEQ ID NO: 278 and Figures 1A and 1B; "Position": position of the corresponding residue within SEQ ID NO: 278 and Figures 1A and 1B; I: Alpha, Regions - Garnier-Robson; II: Alpha, Regions - Chou-Fasman; III: Beta, Regions - Garnier-Robson; IV: Beta, Regions - Chou-Fasman; V: Turn, Regions - Garnier-Robson; VI: Turn, Regions - Chou-Fasman; VII: Coil, Regions - Garnier-Robson; VIII: Hydrophilicity Plot - Kyte-Doolittle; IX: Hydrophobicity Plot - Hopp-Woods; X: Alpha, Amphipathic Regions - Eisenberg; XI: Beta, Amphipathic Regions - Eisenberg; XII: Flexible Regions - Karplus-Schulz; XIII: Antigenic Index - Jameson-Wolf; and XIV: Surface Probability Plot - Emini.

Preferred embodiments of the invention in this regard include fragments that comprise, or alternatively consisting of, one or more of the following regions: alpha-helix and alpha-helix forming regions ("alpha-regions"), beta-sheet and beta-sheet forming regions ("beta-regions"), turn and turn-forming regions ("turn-regions"), coil and coil-forming regions ("coil-regions"), hydrophilic regions, hydrophobic regions, alpha amphipathic regions, beta amphipathic regions, flexible regions, surface-forming regions and high antigenic index regions. The data representing the structural or functional attributes of the protein set forth in Figure 2 and/or Table 3, as described above, was generated using the various modules and algorithms of the DNA*STAR set on default parameters. In a preferred embodiment, the data presented in columns VIII, IX, XIII, and XIV of Table 3 can be used to determine regions of the protein which exhibit a high degree of potential for antigenicity. Regions of high antigenicity are determined from the data presented in columns VIII, IX, XIII, and/or XIV by choosing values which represent regions of the polypeptide which are likely to be exposed on the surface of the polypeptide in an environment in which antigen recognition may occur in the process of initiation of an immune response.

Certain preferred regions in these regards are set out in Figure 2, but may, as shown in Table 3, be represented or identified by using tabular representations of the data presented in Figure 2. The DNA*STAR computer algorithm used to generate Figure 2 (set on the original default parameters) was used to present the data in Figure 2 in a tabular format (See Table 3). The tabular format of the data in Figure 2 is used to easily determine specific boundaries of a preferred region.

The present invention is further directed to fragments of the polynucleotide sequences described herein. By a fragment of, for example, the polynucleotide sequence of a deposited cDNA or the nucleotide sequence shown in SEQ ID NO:40, is intended polynucleotide fragments at least about 15nt, and more preferably at least about 20 nt, at least about 25nt, still more preferably at least about 30 nt, at least about 35nt, and even more preferably, at least about 40 nt in length, at least about 45nt in length, at least about 50nt in length, at least about 60nt in length, at least about 70nt in length, at least about 80nt in length, at least about 90nt in length, at least about 100nt in length, at least about 125nt in length, at least about 150nt in length, at least about 175nt in length, which are useful as diagnostic probes and primers as discussed herein. Of course, larger fragments 200-1500 nt in length are also useful according to the present invention, as are fragments corresponding to most, if not all, of the nucleotide sequence of a deposited cDNA or as shown in SEQ ID NO:40. By a fragment at least 20 nt in length, for example, is intended fragments which include 20 or more contiguous bases from the nucleotide sequence of a deposited cDNA or the nucleotide sequence as shown in SEQ ID NO:40. In this context "about" includes the particularly recited size, an sizes larger or smaller by several (5, 4, 3, 2, or 1) nucleotides, at either terminus or at both termini. Representative examples of polynucleotide fragments of the invention include, for example, fragments that comprise, or alternatively, consist of, a sequence from about nucleotide 1 to about 50, from about 51 to about 100, from about 101 to about 150, from about 151 to about 200, from about 201 to about 250, from about 251 to about 300, from about 301 to about 350, from about 351 to about 400, from about 401 to about 450, from about 451 to about 500, and from about 501 to about 550, and from about 551 to about 600, from about 601 to about 650, from about 651 to about 700, from about 701 to about 750, from about 751 to about 800, from about 801 to about 850, from about 851 to

about 900, from about 901 to about 950, from about 951 to about 1000, from about 1001 to about 1050, from about 1051 to about 1100, from about 1101 to about 1150 from about 1151 to about 1200, from about 1201 to about 1250, from about 1251 to about 1300, from about 1301 to about 1350, from about 1351 to about 1400, from about 1401 to about 1450, and from about 1451 to about 1515, of SEQ ID NO:40, or the complementary strand thereto, or the cDNA contained in a deposited clone. In this context "about" includes the particularly recited ranges, and ranges larger or smaller by several (5, 4, 3, 2, or 1) nucleotides, at either terminus or at both termini. In additional embodiments, the polynucleotides of the invention encode functional attributes of the corresponding protein.

Preferred polypeptide fragments of the invention comprise, or alternatively consist of, the secreted protein having a continuous series of deleted residues from the amino or the carboxyl terminus, or both. Particularly, N-terminal deletions of the polypeptide can be described by the general formula m-362 where m is an integer from 2 to 356, where m corresponds to the position of the amino acid residue identified in SEQ ID NO:278. More in particular, the invention provides polynucleotides encoding polypeptides comprising, or alternatively consisting of, an amino acid sequence selected from the group: K-23 to L-362; S-24 to L-362; D-25 to L-362; A-26 to L-362; K-27 to L-362; K-28 to L-362; A-29 to L-362; A-30 to L-362; S-31 to L-362; K-32 to L-362; T-33 to L-362; L-34 to L-362; L-35 to L-362; E-36 to L-362; K-37 to L-362; S-38 to L-362; Q-39 to L-362; F-40 to L-362; S-41 to L-362; D-42 to L-362; K-43 to L-362; P-44 to L-362; V-45 to L-362; Q-46 to L-362; D-47 to L-362; R-48 to L-362; G-49 to L-362; L-50 to L-362; V-51 to L-362; V-52 to L-362; T-53 to L-362; D-54 to L-362; L-55 to L-362; K-56 to L-362; A-57 to L-362; E-58 to L-362; S-59 to L-362; V-60 to L-362; V-61 to L-362; L-62 to L-362; E-63 to L-362; H-64 to L-362; R-65 to L-362; S-66 to L-362; Y-67 to L-362; C-68 to L-362; S-69 to L-362; A-70 to L-362; K-71 to L-362; A-72 to L-362; R-73 to L-362; D-74 to L-362; R-75 to L-362; H-76 to L-362; F-77 to L-362; A-78 to L-362; G-79 to L-362; D-80 to L-362; V-81 to L-362; L-82 to L-362; G-83 to L-362; Y-84 to L-362; V-85 to L-362; T-86 to L-362; P-87 to L-362; W-88 to L-362; N-89 to L-362; S-90 to L-362; H-91 to L-362; G-92 to L-362; Y-93 to L-362; D-94 to L-362; V-95 to L-362; T-96 to L-362; K-97 to L-362; V-98 to L-362; F-99 to L-362; G-100 to L-362; S-101 to L-362; K-

102 to L-362; F-103 to L-362; T-104 to L-362; Q-105 to L-362; I-106 to L-362; S-107 to L-362; P-108 to L-362; V-109 to L-362; W-110 to L-362; L-111 to L-362; Q-112 to L-362; L-113 to L-362; K-114 to L-362; R-115 to L-362; R-116 to L-362; G-117 to L-362; R-118 to L-362; E-119 to L-362; M-120 to L-362; F-121 to L-362; E-122 to L-362; V-123 to L-362; T-124 to L-362; G-125 to L-362; L-126 to L-362; H-127 to L-362; D-128 to L-362; V-129 to L-362; D-130 to L-362; Q-131 to L-362; G-132 to L-362; W-133 to L-362; M-134 to L-362; R-135 to L-362; A-136 to L-362; V-137 to L-362; R-138 to L-362; K-139 to L-362; H-140 to L-362; A-141 to L-362; K-142 to L-362; G-143 to L-362; L-144 to L-362; H-145 to L-362; I-146 to L-362; V-147 to L-362; P-148 to L-362; R-149 to L-362; L-150 to L-362; L-151 to L-362; F-152 to L-362; E-153 to L-362; D-154 to L-362; W-155 to L-362; T-156 to L-362; Y-157 to L-362; D-158 to L-362; D-159 to L-362; F-160 to L-362; R-161 to L-362; N-162 to L-362; V-163 to L-362; L-164 to L-362; D-165 to L-362; S-166 to L-362; E-167 to L-362; D-168 to L-362; E-169 to L-362; I-170 to L-362; E-171 to L-362; E-172 to L-362; L-173 to L-362; S-174 to L-362; K-175 to L-362; T-176 to L-362; V-177 to L-362; V-178 to L-362; Q-179 to L-362; V-180 to L-362; A-181 to L-362; K-182 to L-362; N-183 to L-362; Q-184 to L-362; H-185 to L-362; F-186 to L-362; D-187 to L-362; G-188 to L-362; F-189 to L-362; V-190 to L-362; V-191 to L-362; E-192 to L-362; V-193 to L-362; W-194 to L-362; N-195 to L-362; Q-196 to L-362; L-197 to L-362; L-198 to L-362; S-199 to L-362; Q-200 to L-362; K-201 to L-362; R-202 to L-362; V-203 to L-362; T-204 to L-362; D-205 to L-362; Q-206 to L-362; L-207 to L-362; G-208 to L-362; M-209 to L-362; F-210 to L-362; T-211 to L-362; H-212 to L-362; K-213 to L-362; E-214 to L-362; F-215 to L-362; E-216 to L-362; Q-217 to L-362; L-218 to L-362; A-219 to L-362; P-220 to L-362; V-221 to L-362; L-222 to L-362; D-223 to L-362; G-224 to L-362; F-225 to L-362; S-226 to L-362; L-227 to L-362; M-228 to L-362; T-229 to L-362; Y-230 to L-362; D-231 to L-362; Y-232 to L-362; S-233 to L-362; T-234 to L-362; A-235 to L-362; H-236 to L-362; Q-237 to L-362; P-238 to L-362; G-239 to L-362; P-240 to L-362; N-241 to L-362; A-242 to L-362; P-243 to L-362; L-244 to L-362; S-245 to L-362; W-246 to L-362; V-247 to L-362; R-248 to L-362; A-249 to L-362; C-250 to L-362; V-251 to L-362; Q-252 to L-362; V-253 to L-362; L-254 to L-362; D-255 to L-362; P-256 to L-362; K-257 to L-362; S-258 to L-362; K-259 to L-362; W-260 to L-362; R-261 to L-362; S-

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262 to L-362; K-263 to L-362; I-264 to L-362; L-265 to L-362; L-266 to L-362; G-267 to L-362; L-268 to L-362; N-269 to L-362; F-270 to L-362; Y-271 to L-362; G-272 to L-362; M-273 to L-362; D-274 to L-362; Y-275 to L-362; A-276 to L-362; T-277 to L-362; S-278 to L-362; K-279 to L-362; D-280 to L-362; A-281 to L-362; R-282 to L-362; E-283 to L-362; P-284 to L-362; V-285 to L-362; V-286 to L-362; G-287 to L-362; A-288 to L-362; R-289 to L-362; Y-290 to L-362; I-291 to L-362; Q-292 to L-362; T-293 to L-362; L-294 to L-362; K-295 to L-362; D-296 to L-362; H-297 to L-362; R-298 to L-362; P-299 to L-362; R-300 to L-362; M-301 to L-362; V-302 to L-362; W-303 to L-362; D-304 to L-362; S-305 to L-362; Q-306 to L-362; X-307 to L-362; S-308 to L-362; E-309 to L-362; H-310 to L-362; F-311 to L-362; F-312 to L-362; E-313 to L-362; Y-314 to L-362; K-315 to L-362; K-316 to L-362; S-317 to L-362; R-318 to L-362; S-319 to L-362; G-320 to L-362; R-321 to L-362; H-322 to L-362; V-323 to L-362; V-324 to L-362; F-325 to L-362; Y-326 to L-362; P-327 to L-362; T-328 to L-362; L-329 to L-362; K-330 to L-362; S-331 to L-362; L-332 to L-362; Q-333 to L-362; V-334 to L-362; R-335 to L-362; L-336 to L-362; E-337 to L-362; L-338 to L-362; A-339 to L-362; R-340 to L-362; E-341 to L-362; L-342 to L-362; G-343 to L-362; V-344 to L-362; G-345 to L-362; V-346 to L-362; S-347 to L-362; I-348 to L-362; W-349 to L-362; E-350 to L-362; L-351 to L-362; G-352 to L-362; Q-353 to L-362; G-354 to L-362; L-355 to L-362; D-356 to L-362; and Y-357 to L-362 of SEQ ID NO:278. Polypeptides encoded by these polynucleotides are also encompassed by the invention.

Additionally, the invention provides polynucleotides encoding polypeptides comprising, or alternatively consisting of, an amino acid sequence selected from the group: R-2 to H-307; T-3 to H-307; L-4 to H-307; F-5 to H-307; N-6 to H-307; L-7 to H-307; L-8 to H-307; W-9 to H-307; L-10 to H-307; A-11 to H-307; L-12 to H-307; A-13 to H-307; C-14 to H-307; S-15 to H-307; P-16 to H-307; V-17 to H-307; H-18 to H-307; T-19 to H-307; T-20 to H-307; L-21 to H-307; S-22 to H-307; K-23 to H-307; S-24 to H-307; D-25 to H-307; A-26 to H-307; K-27 to H-307; K-28 to H-307; A-29 to H-307; A-30 to H-307; S-31 to H-307; K-32 to H-307; T-33 to H-307; L-34 to H-307; L-35 to H-307; E-36 to H-307; K-37 to H-307; S-38 to H-307; Q-39 to H-307; F-40 to H-307; S-41 to H-307; D-42 to H-307; K-43 to H-307; P-44 to H-307; V-45 to H-307; Q-46 to H-307; D-47 to H-307; R-48 to H-307; G-49 to H-307;

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L-50 to H-307; V-51 to H-307; V-52 to H-307; T-53 to H-307; D-54 to H-307; L-55 to H-307; K-56 to H-307; A-57 to H-307; E-58 to H-307; S-59 to H-307; V-60 to H-307; V-61 to H-307; L-62 to H-307; E-63 to H-307; H-64 to H-307; R-65 to H-307; S-66 to H-307; Y-67 to H-307; C-68 to H-307; S-69 to H-307; A-70 to H-307; K-71 to H-307; A-72 to H-307; R-73 to H-307; D-74 to H-307; R-75 to H-307; H-76 to H-307; F-77 to H-307; A-78 to H-307; G-79 to H-307; D-80 to H-307; V-81 to H-307; L-82 to H-307; G-83 to H-307; Y-84 to H-307; V-85 to H-307; T-86 to H-307; P-87 to H-307; W-88 to H-307; N-89 to H-307; S-90 to H-307; H-91 to H-307; G-92 to H-307; Y-93 to H-307; D-94 to H-307; V-95 to H-307; T-96 to H-307; K-97 to H-307; V-98 to H-307; F-99 to H-307; G-100 to H-307; S-101 to H-307; K-102 to H-307; F-103 to H-307; T-104 to H-307; Q-105 to H-307; I-106 to H-307; S-107 to H-307; P-108 to H-307; V-109 to H-307; W-110 to H-307; L-111 to H-307; Q-112 to H-307; L-113 to H-307; K-114 to H-307; R-115 to H-307; R-116 to H-307; G-117 to H-307; R-118 to H-307; E-119 to H-307; M-120 to H-307; F-121 to H-307; E-122 to H-307; V-123 to H-307; T-124 to H-307; G-125 to H-307; L-126 to H-307; H-127 to H-307; D-128 to H-307; V-129 to H-307; D-130 to H-307; Q-131 to H-307; G-132 to H-307; W-133 to H-307; M-134 to H-307; R-135 to H-307; A-136 to H-307; V-137 to H-307; R-138 to H-307; K-139 to H-307; H-140 to H-307; A-141 to H-307; K-142 to H-307; G-143 to H-307; L-144 to H-307; H-145 to H-307; I-146 to H-307; V-147 to H-307; P-148 to H-307; R-149 to H-307; L-150 to H-307; L-151 to H-307; F-152 to H-307; E-153 to H-307; D-154 to H-307; W-155 to H-307; T-156 to H-307; Y-157 to H-307; D-158 to H-307; D-159 to H-307; F-160 to H-307; R-161 to H-307; N-162 to H-307; V-163 to H-307; L-164 to H-307; D-165 to H-307; S-166 to H-307; E-167 to H-307; D-168 to H-307; E-169 to H-307; I-170 to H-307; E-171 to H-307; E-172 to H-307; L-173 to H-307; S-174 to H-307; K-175 to H-307; T-176 to H-307; V-177 to H-307; V-178 to H-307; Q-179 to H-307; V-180 to H-307; A-181 to H-307; K-182 to H-307; N-183 to H-307; Q-184 to H-307; H-185 to H-307; F-186 to H-307; D-187 to H-307; G-188 to H-307; F-189 to H-307; V-190 to H-307; V-191 to H-307; E-192 to H-307; V-193 to H-307; W-194 to H-307; N-195 to H-307; Q-196 to H-307; L-197 to H-307; L-198 to H-307; S-199 to H-307; Q-200 to H-307; K-201 to H-307; R-202 to H-307; V-203 to H-307; G-204 to H-307; L-205 to H-307; I-206 to H-307; H-207 to H-307; M-208 to H-307; L-209 to H-307; T-210 to H-307; H-211 to H-307; L-212 to

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H-307; A-213 to H-307; E-214 to H-307; A-215 to H-307; L-216 to H-307; H-217 to H-307; Q-218 to H-307; A-219 to H-307; R-220 to H-307; L-221 to H-307; L-222 to H-307; A-223 to H-307; L-224 to H-307; L-225 to H-307; V-226 to H-307; I-227 to H-307; P-228 to H-307; P-229 to H-307; A-230 to H-307; I-231 to H-307; T-232 to H-307; P-233 to H-307; G-234 to H-307; T-235 to H-307; D-236 to H-307; Q-237 to H-307; L-238 to H-307; G-239 to H-307; M-240 to H-307; F-241 to H-307; T-242 to H-307; H-243 to H-307; K-244 to H-307; E-245 to H-307; F-246 to H-307; E-247 to H-307; Q-248 to H-307; L-249 to H-307; A-250 to H-307; P-251 to H-307; V-252 to H-307; L-253 to H-307; D-254 to H-307; G-255 to H-307; F-256 to H-307; S-257 to H-307; L-258 to H-307; M-259 to H-307; T-260 to H-307; Y-261 to H-307; D-262 to H-307; Y-263 to H-307; S-264 to H-307; T-265 to H-307; A-266 to H-307; H-267 to H-307; Q-268 to H-307; P-269 to H-307; G-270 to H-307; P-271 to H-307; N-272 to H-307; A-273 to H-307; P-274 to H-307; L-275 to H-307; S-276 to H-307; W-277 to H-307; V-278 to H-307; R-279 to H-307; A-280 to H-307; C-281 to H-307; V-282 to H-307; Q-283 to H-307; V-284 to H-307; L-285 to H-307; D-286 to H-307; P-287 to H-307; K-288 to H-307; S-289 to H-307; K-290 to H-307; W-291 to H-307; R-292 to H-307; S-293 to H-307; K-294 to H-307; I-295 to H-307; L-296 to H-307; L-297 to H-307; G-298 to H-307; L-299 to H-307; N-300 to H-307; F-301 to H-307; and Y-302 to H-307 of SEQ ID NO: 1232. Polypeptides encoded by these polynucleotides are also encompassed by the invention.

Also as mentioned above, even if deletion of one or more amino acids from the C-terminus of a protein results in modification of loss of one or more biological functions of the protein (e.g., ability to inhibit the Mixed Lymphocyte Reaction), other functional activities (e.g., biological activities, ability to multimerize, ability to bind ligand, ability to generate antibodies, ability to bind antibodies) may still be retained. For example the ability of the shortened polypeptide to induce and/or bind to antibodies which recognize the complete or mature forms of the polypeptide generally will be retained when less than the majority of the residues of the complete or mature polypeptide are removed from the C-terminus. Whether a particular polypeptide lacking C-terminal residues of a complete polypeptide retains such immunologic activities can readily be determined by routine methods described herein and otherwise known in the art. It is not unlikely that a polypeptide with a

large number of deleted C-terminal amino acid residues may retain some biological or immunogenic activities. In fact, peptides composed of as few as six amino acid residues may often evoke an immune response.

Accordingly, the present invention further provides polypeptides having one or more residues deleted from the carboxyl terminus of the amino acid sequence of the polypeptide shown in Figures 1A-B (SEQ ID NO:278), as described by the general formula 1-n, where n is an integer from 6 to 356, where n corresponds to the position of the amino acid residue identified in SEQ ID NO:278. More in particular, the invention provides polynucleotides encoding polypeptides comprising, or alternatively consisting of, an amino acid sequence selected from the group: K-23 to L-362; K-23 to L-361; K-23 to D-360; K-23 to Y-359; K-23 to F-358; K-23 to Y-357; K-23 to D-356; K-23 to L-355; K-23 to G-354; K-23 to Q-353; K-23 to G-352; K-23 to L-351; K-23 to E-350; K-23 to W-349; K-23 to I-348; K-23 to S-347; K-23 to V-346; K-23 to G-345; K-23 to V-344; K-23 to G-343; K-23 to L-342; K-23 to E-341; K-23 to R-340; K-23 to A-339; K-23 to L-338; K-23 to E-337; K-23 to L-336; K-23 to R-335; K-23 to V-334; K-23 to Q-333; K-23 to L-332; K-23 to S-331; K-23 to K-330; K-23 to L-329; K-23 to T-328; K-23 to P-327; K-23 to Y-326; K-23 to F-325; K-23 to V-324; K-23 to V-323; K-23 to H-322; K-23 to R-321; K-23 to G-320; K-23 to S-319; K-23 to R-318; K-23 to S-317; K-23 to K-316; K-23 to K-315; K-23 to Y-314; K-23 to E-313; K-23 to F-312; K-23 to F-311; K-23 to H-310; K-23 to E-309; K-23 to S-308; K-23 to X-307; K-23 to Q-306; K-23 to S-305; K-23 to D-304; K-23 to W-303; K-23 to V-302; K-23 to M-301; K-23 to R-300; K-23 to P-299; K-23 to R-298; K-23 to H-297; K-23 to D-296; K-23 to K-295; K-23 to L-294; K-23 to T-293; K-23 to Q-292; K-23 to I-291; K-23 to Y-290; K-23 to R-289; K-23 to A-288; K-23 to G-287; K-23 to V-286; K-23 to V-285; K-23 to P-284; K-23 to E-283; K-23 to R-282; K-23 to A-281; K-23 to D-280; K-23 to K-279; K-23 to S-278; K-23 to T-277; K-23 to A-276; K-23 to Y-275; K-23 to D-274; K-23 to M-273; K-23 to G-272; K-23 to Y-271; K-23 to F-270; K-23 to N-269; K-23 to L-268; K-23 to G-267; K-23 to L-266; K-23 to L-265; K-23 to I-264; K-23 to K-263; K-23 to S-262; K-23 to R-261; K-23 to W-260; K-23 to K-259; K-23 to S-258; K-23 to K-257; K-23 to P-256; K-23 to D-255; K-23 to L-254; K-23 to V-253; K-23 to Q-252; K-23 to V-251; K-23 to C-250; K-23 to A-249; K-23 to R-248; K-23 to V-247; K-23 to W-246; K-23 to S-245;

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K-23 to L-244; K-23 to P-243; K-23 to A-242; K-23 to N-241; K-23 to P-240; K-23 to G-239; K-23 to P-238; K-23 to Q-237; K-23 to H-236; K-23 to A-235; K-23 to T-234; K-23 to S-233; K-23 to Y-232; K-23 to D-231; K-23 to Y-230; K-23 to T-229; K-23 to M-228; K-23 to L-227; K-23 to S-226; K-23 to F-225; K-23 to G-224; K-23 to D-223; K-23 to L-222; K-23 to V-221; K-23 to P-220; K-23 to A-219; K-23 to L-218; K-23 to Q-217; K-23 to E-216; K-23 to F-215; K-23 to E-214; K-23 to K-213; K-23 to H-212; K-23 to T-211; K-23 to F-210; K-23 to M-209; K-23 to G-208; K-23 to L-207; K-23 to Q-206; K-23 to D-205; K-23 to T-204; K-23 to V-203; K-23 to R-202; K-23 to K-201; K-23 to Q-200; K-23 to S-199; K-23 to L-198; K-23 to L-197; K-23 to Q-196; K-23 to N-195; K-23 to W-194; K-23 to V-193; K-23 to E-192; K-23 to V-191; K-23 to V-190; K-23 to F-189; K-23 to G-188; K-23 to D-187; K-23 to F-186; K-23 to H-185; K-23 to Q-184; K-23 to N-183; K-23 to K-182; K-23 to A-181; K-23 to V-180; K-23 to Q-179; K-23 to V-178; K-23 to V-177; K-23 to T-176; K-23 to K-175; K-23 to S-174; K-23 to L-173; K-23 to E-172; K-23 to E-171; K-23 to I-170; K-23 to E-169; K-23 to D-168; K-23 to E-167; K-23 to S-166; K-23 to D-165; K-23 to L-164; K-23 to V-163; K-23 to N-162; K-23 to R-161; K-23 to F-160; K-23 to D-159; K-23 to D-158; K-23 to Y-157; K-23 to T-156; K-23 to W-155; K-23 to D-154; K-23 to E-153; K-23 to F-152; K-23 to L-151; K-23 to L-150; K-23 to R-149; K-23 to P-148; K-23 to V-147; K-23 to I-146; K-23 to H-145; K-23 to L-144; K-23 to G-143; K-23 to K-142; K-23 to A-141; K-23 to H-140; K-23 to K-139; K-23 to R-138; K-23 to V-137; K-23 to A-136; K-23 to R-135; K-23 to M-134; K-23 to W-133; K-23 to G-132; K-23 to Q-131; K-23 to D-130; K-23 to V-129; K-23 to D-128; K-23 to H-127; K-23 to L-126; K-23 to G-125; K-23 to T-124; K-23 to V-123; K-23 to E-122; K-23 to F-121; K-23 to M-120; K-23 to E-119; K-23 to R-118; K-23 to G-117; K-23 to R-116; K-23 to R-115; K-23 to K-114; K-23 to L-113; K-23 to Q-112; K-23 to L-111; K-23 to W-110; K-23 to V-109; K-23 to P-108; K-23 to S-107; K-23 to I-106; K-23 to Q-105; K-23 to T-104; K-23 to F-103; K-23 to K-102; K-23 to S-101; K-23 to G-100; K-23 to F-99; K-23 to V-98; K-23 to K-97; K-23 to T-96; K-23 to V-95; K-23 to D-94; K-23 to Y-93; K-23 to G-92; K-23 to H-91; K-23 to S-90; K-23 to N-89; K-23 to W-88; K-23 to P-87; K-23 to T-86; K-23 to V-85; K-23 to Y-84; K-23 to G-83; K-23 to L-82; K-23 to V-81; K-23 to D-80; K-23 to G-79; K-23 to A-78; K-23 to F-77; K-23 to H-76; K-23 to R-75; K-23 to D-74; K-23 to R-73; K-23 to A-72;

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K-23 to K-71; K-23 to A-70; K-23 to S-69; K-23 to C-68; K-23 to Y-67; K-23 to S-66; K-23 to R-65; K-23 to H-64; K-23 to E-63; K-23 to L-62; K-23 to V-61; K-23 to V-60; K-23 to S-59; K-23 to E-58; K-23 to A-57; K-23 to K-56; K-23 to L-55; K-23 to D-54; K-23 to T-53; K-23 to V-52; K-23 to V-51; K-23 to L-50; K-23 to G-49; K-23 to R-48; K-23 to D-47; K-23 to Q-46; K-23 to V-45; K-23 to P-44; K-23 to K-43; K-23 to D-42; K-23 to S-41; K-23 to F-40; K-23 to Q-39; K-23 to S-38; K-23 to K-37; K-23 to E-36; K-23 to L-35; K-23 to L-34; K-23 to T-33; K-23 to K-32; K-23 to S-31; K-23 to A-30; and K-23 to A-29 of SEQ ID NO:278. Polypeptides encoded by these polynucleotides are also encompassed by the invention.

Additionally, the invention provides polynucleotides encoding polypeptides comprising, or alternatively consisting of, an amino acid sequence selected from the group: K-23 to R-306; K-23 to S-305; K-23 to T-304; K-23 to G-303; K-23 to Y-302; K-23 to F-301; K-23 to N-300; K-23 to L-299; K-23 to G-298; K-23 to L-297; K-23 to L-296; K-23 to I-295; K-23 to K-294; K-23 to S-293; K-23 to R-292; K-23 to W-291; K-23 to K-290; K-23 to S-289; K-23 to K-288; K-23 to P-287; K-23 to D-286; K-23 to L-285; K-23 to V-284; K-23 to Q-283; K-23 to V-282; K-23 to C-281; K-23 to A-280; K-23 to R-279; K-23 to V-278; K-23 to W-277; K-23 to S-276; K-23 to L-275; K-23 to P-274; K-23 to A-273; K-23 to N-272; K-23 to P-271; K-23 to G-270; K-23 to P-269; K-23 to Q-268; K-23 to H-267; K-23 to A-266; K-23 to T-265; K-23 to S-264; K-23 to Y-263; K-23 to D-262; K-23 to Y-261; K-23 to T-260; K-23 to M-259; K-23 to L-258; K-23 to S-257; K-23 to F-256; K-23 to G-255; K-23 to D-254; K-23 to L-253; K-23 to V-252; K-23 to P-251; K-23 to A-250; K-23 to L-249; K-23 to Q-248; K-23 to E-247; K-23 to F-246; K-23 to E-245; K-23 to K-244; K-23 to H-243; K-23 to T-242; K-23 to F-241; K-23 to M-240; K-23 to G-239; K-23 to L-238; K-23 to Q-237; K-23 to D-236; K-23 to T-235; K-23 to G-234; K-23 to P-233; K-23 to T-232; K-23 to I-231; K-23 to A-230; K-23 to P-229; K-23 to P-228; K-23 to I-227; K-23 to V-226; K-23 to L-225; K-23 to L-224; K-23 to A-223; K-23 to L-222; K-23 to L-221; K-23 to R-220; K-23 to A-219; K-23 to Q-218; K-23 to H-217; K-23 to L-216; K-23 to A-215; K-23 to E-214; K-23 to A-213; K-23 to L-212; K-23 to H-211; K-23 to T-210; K-23 to L-209; K-23 to M-208; K-23 to H-207; K-23 to I-206; K-23 to L-205; K-23 to G-204; K-23 to V-203; K-23 to R-202; K-23 to K-201; K-23 to Q-200; K-23 to S-199; K-23 to L-198; K-23 to L-197; K-23 to Q-196; K-23 to N-

195; K-23 to W-194; K-23 to V-193; K-23 to E-192; K-23 to V-191; K-23 to V-190; K-23 to F-189; K-23 to G-188; K-23 to D-187; K-23 to F-186; K-23 to H-185; K-23 to Q-184; K-23 to N-183; K-23 to K-182; K-23 to A-181; K-23 to V-180; K-23 to Q-179; K-23 to V-178; K-23 to V-177; K-23 to T-176; K-23 to K-175; K-23 to S-174; K-23 to L-173; K-23 to E-172; K-23 to E-171; K-23 to I-170; K-23 to E-169; K-23 to D-168; K-23 to E-167; K-23 to S-166; K-23 to D-165; K-23 to L-164; K-23 to V-163; K-23 to N-162; K-23 to R-161; K-23 to F-160; K-23 to D-159; K-23 to D-158; K-23 to Y-157; K-23 to T-156; K-23 to W-155; K-23 to D-154; K-23 to E-153; K-23 to F-152; K-23 to L-151; K-23 to L-150; K-23 to R-149; K-23 to P-148; K-23 to V-147; K-23 to I-146; K-23 to H-145; K-23 to L-144; K-23 to G-143; K-23 to K-142; K-23 to A-141; K-23 to H-140; K-23 to K-139; K-23 to R-138; K-23 to V-137; K-23 to A-136; K-23 to R-135; K-23 to M-134; K-23 to W-133; K-23 to G-132; K-23 to Q-131; K-23 to D-130; K-23 to V-129; K-23 to D-128; K-23 to H-127; K-23 to L-126; K-23 to G-125; K-23 to T-124; K-23 to V-123; K-23 to E-122; K-23 to F-121; K-23 to M-120; K-23 to E-119; K-23 to R-118; K-23 to G-117; K-23 to R-116; K-23 to R-115; K-23 to K-114; K-23 to L-113; K-23 to Q-112; K-23 to L-111; K-23 to W-110; K-23 to V-109; K-23 to P-108; K-23 to S-107; K-23 to I-106; K-23 to Q-105; K-23 to T-104; K-23 to F-103; K-23 to K-102; K-23 to S-101; K-23 to G-100; K-23 to F-99; K-23 to V-98; K-23 to K-97; K-23 to T-96; K-23 to V-95; K-23 to D-94; K-23 to Y-93; K-23 to G-92; K-23 to H-91; K-23 to S-90; K-23 to N-89; K-23 to W-88; K-23 to P-87; K-23 to T-86; K-23 to V-85; K-23 to Y-84; K-23 to G-83; K-23 to L-82; K-23 to V-81; K-23 to D-80; K-23 to G-79; K-23 to A-78; K-23 to F-77; K-23 to H-76; K-23 to R-75; K-23 to D-74; K-23 to R-73; K-23 to A-72; K-23 to K-71; K-23 to A-70; K-23 to S-69; K-23 to C-68; K-23 to Y-67; K-23 to S-66; K-23 to R-65; K-23 to H-64; K-23 to E-63; K-23 to L-62; K-23 to V-61; K-23 to V-60; K-23 to S-59; K-23 to E-58; K-23 to A-57; K-23 to K-56; K-23 to L-55; K-23 to D-54; K-23 to T-53; K-23 to V-52; K-23 to V-51; K-23 to L-50; K-23 to G-49; K-23 to R-48; K-23 to D-47; K-23 to Q-46; K-23 to V-45; K-23 to P-44; K-23 to K-43; K-23 to D-42; K-23 to S-41; K-23 to F-40; K-23 to Q-39; K-23 to S-38; K-23 to K-37; K-23 to E-36; K-23 to L-35; K-23 to L-34; K-23 to T-33; K-23 to K-32; K-23 to S-31; K-23 to A-30; and K-23 to A-29 of SEQ ID NO:1232. Polypeptides encoded by these polynucleotides are also encompassed by the invention.

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In addition, any of the above listed N- or C-terminal deletions can be combined to produce a N- and C-terminal deleted polypeptide. The invention also provides polypeptides comprising, or alternatively consisting of, one or more amino acids deleted from both the amino and the carboxyl termini, which may be described generally as having residues m-n of SEQ ID NO:278, where n and m are integers as described above. Polynucleotides encoding these polypeptides are also encompassed by the invention.

The present invention is also directed to proteins containing polypeptides at least 80%, 85%, 90%, 92%, 93%, 94%, 95%, 96%, 97%, 98% or 99% identical to a polypeptide sequence set forth herein as m-n. In preferred embodiments, the application is directed to proteins containing polypeptides at least 80%, 85%, 90%, 95%, 96%, 97%, 98% or 99% identical to polypeptides having the amino acid sequence of the specific N- and C-terminal deletions recited herein. Polynucleotides encoding these polypeptides are also encompassed by the invention.

Also included are polynucleotide sequences encoding a polypeptide consisting of a portion of the complete amino acid sequence encoded by a cDNA clone contained in ATCC Deposit No. 209080, where this portion excludes any integer of amino acid residues from 1 to about 356 amino acids from the amino terminus of the complete amino acid sequence encoded by a cDNA clone contained in ATCC Deposit No. 209080, or any integer of amino acid residues from 1 to about 356 amino acids from the carboxyl terminus, or any combination of the above amino terminal and carboxyl terminal deletions, of the complete amino acid sequence encoded by the cDNA clone contained in ATCC Deposit No. 209080. Polypeptides encoded by these polynucleotides also are encompassed by the invention.

As described herein or otherwise known in the art, the polynucleotides of the invention have uses that include, but are not limited to, serving as probes or primers in chromosome identification, chromosome mapping, and linkage analysis. The gene encoding the disclosed cDNA is thought to reside on chromosome 11. Accordingly, polynucleotides related to this invention have uses, such as, for example, as a marker in linkage analysis for chromosome 11.

Polynucleotides and polypeptides of the invention are useful as reagents for differential identification of the tissue(s) or cell type(s) present in a biological sample

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and for diagnosis of diseases and conditions which include, but are not limited to, immune and gastrointestinal disorders and cancer. Similarly, polypeptides and antibodies directed to these polypeptides are useful in providing immunological probes for differential identification of the tissue(s) or cell type(s). For a number of disorders of the above tissues or cells, particularly of the immune and gastrointestinal systems, expression of this gene at significantly higher or lower levels may be routinely detected in certain tissues or cell types (e.g. immune, cancerous and wounded tissues) or bodily fluids (e.g., lymph, serum, plasma, urine, synovial fluid and spinal fluid) or another tissue or cell sample taken from an individual having such a disorder, relative to the standard gene expression level, i.e., the expression level in healthy tissue or bodily fluid from an individual not having the disorder.

When tested against Jurkat cell lines, supernatants removed from cells expressing this gene activated the nuclear-factor kB (NF-kB) transcription factor. Thus, it is likely that this gene activates Jurkat cells by activating a transcriptional factor found within these cells. Nuclear factor kB is a transcription factor activated by a wide variety of agents, leading to cell activation, differentiation, or apoptosis. Reporter constructs utilizing the NF-kB promoter element were used to screen supernatants for such activity.

Additionally, products of this gene have been found to inhibit the Mixed Lymphocyte Reaction (MLR). This assay is described in Example 58 herein. Inhibition of a MLR may be due to a direct effect on cell proliferation and viability, modulation of costimulatory molecules on interacting cells, modulation of adhesiveness between lymphocytes and accessory cells, or modulation of cytokine production by accessory cells. Multiple cells may be targeted by these polypeptides since the peripheral blood mononuclear fraction used in this assay includes T, B and natural killer lymphocytes, as well as monocytes and dendritic cells.

The tissue distribution in immune cells (e.g., T-cells, macrophages) and inhibition of the MLR indicates that the polynucleotides and polypeptides corresponding to this gene are useful for the diagnosis, treatment, and/or prevention of many diseases associated with lymphocyte and monocyte activation or proliferation. These include, but are not limited to, diseases such as asthma, arthritis, diabetes, inflammatory skin conditions, psoriasis, eczema, systemic lupus

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erythematosus, multiple sclerosis, glomerulonephritis, inflammatory bowel disease, Crohn's disease, ulcerative colitis, arteriosclerosis, cirrhosis, graft vs. host disease, host vs. graft disease, hepatitis, leukemia and lymphoma. Since the gene is expressed in cells of lymphoid origin, the natural gene product may be involved in immune functions. Therefore, polynucleotides and polypeptides of the invention (including fragments, variants, and derivatives) may be also used to treat, prevent and/or diagnose immunological disorders including, but not limited to, arthritis, asthma, immunodeficiency diseases such as AIDS, leukemia, rheumatoid arthritis, granulomatous disease, inflammatory bowel disease, sepsis, acne, neutropenia, neutrophilia, psoriasis, hypersensitivities, such as T-cell mediated cytotoxicity; immune reactions to transplanted organs and tissues, such as host-versus-graft and graft-versus-host diseases, or autoimmunity disorders, such as autoimmune infertility, lens tissue injury, demyelination, systemic lupus erythematosis, drug induced hemolytic anemia, rheumatoid arthritis, Sjogren's disease, and scleroderma.

The tissue distribution in human T-cells and human colon carcinoma indicates that the polynucleotides and polypeptides corresponding to this gene are useful for the diagnosis, treatment, and/or prevention of immune disorders and gastrointestinal diseases. Non-limiting representative uses for these polynucleotides and polypeptides are described in the "Immune Activity" and "Infectious Disease" sections below, in Example 11, 13, 14, 16, 18, 19, 20, and 27, and elsewhere herein. Furthermore, this gene product may be involved in the regulation of cytokine production, antigen presentation, or other processes that may also suggest a usefulness in the treatment of cancer (e.g. by boosting immune responses). Since the gene is expressed in cells of lymphoid origin, the gene or protein, as well as, antibodies directed against the protein may as be useful as a tumor marker and/or immunotherapy targets for the above listed tissues. In addition, polynucleotides and polypeptides of the invention may have commercial utility in the expansion of stem cells and committed progenitors of various blood lineages, in the differentiation and/or proliferation of various cell types (e.g., T, B and natural killer lymphocytes, monocytes, dendritic cells), modulation of costimulatory molecules on interacting cells, modulation of adhesiveness between lymphocytes and accessory cells, and/or modulation of cytokine production by accessory cells.

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Furthermore, the protein may also be used to determine biological activity, to raise antibodies, as tissue markers, to isolate cognate ligands or receptors, to identify agents that modulate their interactions, in addition to its use as a nutritional supplement.

Many polynucleotide sequences, such as EST sequences, are publicly available and accessible through sequence databases. Some of these sequences are related to SEQ ID NO:40 and may have been publicly available prior to conception of the present invention. Preferably, such related polynucleotides are specifically excluded from the scope of the present invention. To list every related sequence is cumbersome. Accordingly, preferably excluded from the present invention are one or more polynucleotides comprising a nucleotide sequence described by the general formula of a-b, where a is any integer between 1 to 1501 of SEQ ID NO:40, b is an integer of 15 to 1515, where both a and b correspond to the positions of nucleotide residues shown in SEQ ID NO:40, and where b is greater than or equal to a + 14.

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FEATURES OF PROTEIN ENCODED BY GENE NO: 31

The translation product of this gene shares sequence homology with Ribosomal protein L11 of Caenorhabditis elegans. (See Genbank Accession No. 156201.)

In specific embodiments, polypeptides of the invention comprise, or alternatively consists of, an amino acid sequence selected from the group: ERGVSINQFCKEFNERTKDIKEGIPLPTKILVKPDRTFEIKIGQPTVSYFLKAAA GI EKGARQTGKEVAGLVTLKHVYEIARIKAQDEAFALQDVPLSSVVRSIIG SARSLGIRVVKDLSSEELAAF QKERAIFLAAQKEADLAAQEEAAKK (SEQ ID NO:564), ERGVSINQFCKEFNERTKDIKEGIPLPTKILVKPDRTFEIKIGQ PTVSYFL (SEQ ID NO:565), KAAAGIEKGARQTGKEVAGLVTLKHVYEIARIK AQDEAFALQDVPLSSV (SEQ ID NO:566), and/or VRSIIGSARSLGIRVVK DLSSEELAAFQKERAIFLAAQKEADLAAQEEAAKK (SEQ ID NO:567).

Moreover, fragments and variants of these polypeptides (such as, for example, fragments as described herein, polypeptides at least 80%, 85%, 90%, 95%, 96%, 97%, 98%, or 99% identical to these polypeptides and polypeptides encoded by the polynucleotide which hybridizes, under stringent conditions, to the polynucleotide

encoding these polypeptides) are encompassed by the invention. Antibodies that bind polypeptides of the invention are also encompassed by the invention. Polynucleotides encoding these polypeptides are also encompassed by the invention.

The gene encoding the disclosed cDNA is thought to reside on chromosome 11. Accordingly, polynucleotides related to this invention are useful as a marker in linkage analysis for chromosome 11.

This gene is expressed in human embryo tissue, and to a lesser extent, in human epithelioid sarcoma.

Therefore, polynucleotides and polypeptides of the invention are useful as reagents for identification of the tissue(s) or cell type(s) present in a biological sample and for diagnosis of diseases and conditions which include, but are not limited to, development disorders and epithelial cell cancer. Similarly, polypeptides and antibodies directed to these polypeptides are useful in providing immunological probes for differential identification of the tissue(s) or cell type(s). For a number of disorders of the above tissues or cells, particularly of the embryonic and epithelial cell systems, expression of this gene at significantly higher or lower levels may be routinely detected in certain tissues or cell types (e.g. embryonic, cancerous and wounded tissues) or bodily fluids (e.g. lymph, serum, plasma, urine, synovial fluid and spinal fluid) or another tissue or cell sample taken from an individual having such a disorder, relative to the standard gene expression level, i.e., the expression level in healthy tissue or bodily fluid from an individual not having the disorder.

Predicted epitopes include those comprising a sequence shown in SEQ ID NO: 279 as residues: Lys-34 to Gly-40.

The tissue distribution in human embryo indicates that the protein product of this gene is useful for the diagnosis and treatment of developmental disorders and epithelial cancer. Furthermore, expression within embryonic tissue and other cellular sources marked by proliferating cells indicates that this protein may play a role in the regulation of cellular division, and may show utility in the diagnosis and treatment of cancer and other proliferative disorders. Similarly, embryonic development also involves decisions involving cell differentiation and/or apoptosis in pattern formation. Thus this protein may also be involved in apoptosis or tissue differentiation and could again be useful in cancer therapy. Protein, as well as, antibodies directed against the

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protein may show utility as a tumor marker and/or immunotherapy targets for the above listed tissues.

Many polynucleotide sequences, such as EST sequences, are publicly available and accessible through sequence databases. Some of these sequences are related to SEQ ID NO:41 and may have been publicly available prior to conception of the present invention. Preferably, such related polynucleotides are specifically excluded from the scope of the present invention. To list every related sequence is cumbersome. Accordingly, preferably excluded from the present invention are one or more polynucleotides comprising a nucleotide sequence described by the general formula of a-b, where a is any integer between 1 to 690 of SEQ ID NO:41, b is an integer of 15 to 704, where both a and b correspond to the positions of nucleotide residues shown in SEQ ID NO:41, and where b is greater than or equal to a + 14.

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FEATURES OF PROTEIN ENCODED BY GENE NO: 32

This gene is expressed primarily in resting T-cells.

Polynucleotides and polypeptides of the invention are useful as reagents for differential identification of the tissue(s) or cell type(s) present in a biological sample and for diagnosis of diseases and conditions which include, but are not limited to, inflammatory and general immune disorders. Similarly, polypeptides and antibodies directed to these polypeptides are useful in providing immunological probes for differential identification of the tissue(s) or cell type(s). For a number of disorders of the above tissues or cells, particularly of the immune system, expression of this gene at significantly higher or lower levels may be routinely detected in certain tissues or cell types (e.g. immune, cancerous and wounded tissues) or bodily fluids (e.g. lymph, serum, plasma, urine, synovial fluid and spinal fluid) or another tissue or cell sample taken from an individual having such a disorder, relative to the standard gene expression level, i.e., the expression level in healthy tissue or bodily fluid from an individual not having the disorder.

The tissue distribution in T-cells indicates that the protein product of this gene is useful for the diagnosis and treatment of disorders of the immune system.

Furthermore, this gene product may be involved in the regulation of cytokine production, antigen presentation, or other processes that may also suggest a usefulness in the treatment of cancer (e.g. by boosting immune responses). Since the gene is expressed in cells of lymphoid origin, the gene or protein, as well as, antibodies directed against the protein may show utility as a tumor marker and/or immunotherapy targets for the above listed tissues. Expression of this gene product in T cells also strongly indicates a role for this protein in immune function and immune surveillance.

Many polynucleotide sequences, such as EST sequences, are publicly available and accessible through sequence databases. Some of these sequences are related to SEQ ID NO:42 and may have been publicly available prior to conception of the present invention. Preferably, such related polynucleotides are specifically excluded from the scope of the present invention. To list every related sequence is cumbersome. Accordingly, preferably excluded from the present invention are one or more polynucleotides comprising a nucleotide sequence described by the general formula of a-b, where a is any integer between 1 to 1080 of SEQ ID NO:42, b is an integer of 15 to 1094, where both a and b correspond to the positions of nucleotide residues shown in SEQ ID NO:42, and where b is greater than or equal to a + 14.

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FEATURES OF PROTEIN ENCODED BY GENE NO: 33

This gene is believed to reside on chromosome 1. Accordingly, polynucleotides derived from this gene are useful in linkage analysis as chromosome 1 markers.

This gene is expressed primarily in prostate, and to a lesser extent in soares adult brain, human umbilical vein endothelial cells, and amniotic cells.

Polynucleotides and polypeptides of the invention are useful as reagents for differential identification of the tissue(s) or cell type(s) present in a biological sample and for diagnosis of diseases and conditions which include, but are not limited to, prostate-related disorders. Similarly, polypeptides and antibodies directed to these polypeptides are useful in providing immunological probes for differential

identification of the tissue(s) or cell type(s). For a number of disorders of the above tissues or cells, particularly of the urinary system and nervous system expression of this gene at significantly higher or lower levels may be routinely detected in certain tissues or cell types (e.g. prostate, cancerous and wounded tissues) or bodily fluids (e.g. lymph, serum, plasma, urine, synovial fluid and spinal fluid) or another tissue or cell sample taken from an individual having such a disorder, relative to the standard gene expression level, i.e., the expression level in healthy tissue or bodily fluid from an individual not having the disorder.

The tissue distribution in prostate indicates that the protein products of this gene are useful for the diagnosis and treatment of disorders of the urinary and nervous systems. Furthermore, the tissue distribution indicates that the protein product of this gene is useful for the detection/treatment of neurodegenerative disease states and behavioral disorders such as Alzheimer's Disease, Parkinson's Disease, Huntington's Disease, Tourette's Syndrome, schizophrenia, mania, dementia, paranoia, obsessive compulsive disorder, panic disorder, learning disabilities, ALS, psychoses, autism, and altered behaviors, including disorders in feeding, sleep patterns, balance, and perception. Protein, as well as, antibodies directed against the protein may show utility as a tumor marker and/or immunotherapy targets for the above listed tissues.

Many polynucleotide sequences, such as EST sequences, are publicly available and accessible through sequence databases. Some of these sequences are related to SEQ ID NO:43 and may have been publicly available prior to conception of the present invention. Preferably, such related polynucleotides are specifically excluded from the scope of the present invention. To list every related sequence is cumbersome. Accordingly, preferably excluded from the present invention are one or more polynucleotides comprising a nucleotide sequence described by the general formula of a-b, where a is any integer between 1 to 1807 of SEQ ID NO:43, b is an integer of 15 to 1821, where both a and b correspond to the positions of nucleotide residues shown in SEQ ID NO:43, and where b is greater than or equal to a + 14.

FEATURES OF PROTEIN ENCODED BY GENE NO: 34

This gene shares sequence homology with R05G6.4 gene product. (See Genbank Accession No. gi|1326338.) This gene also shares sequence homology with the cyclophilin-like protein CyP-60. (See Genbank Accession No. 1199598, see also Biochem. J. 314 (1), 313-319 (1996).)

In specific embodiments, polypeptides of the invention comprise, or alternatively consists of, an amino acid sequence selected from the group: AVYTYHEKKKDTAASGYGTQNIRLSRDAVKDFDCCCLSLQPCHDPVVTPDG YLYEREAILEYILHQKKEIARQMKAYEKQRGTRREEQKELQRAASQDHVRGF LEKESAIVSRPLNPFTAKALSGTSPDDVQPGPSVGPPSKDKDKVLPSFWIPSLT PEAKATKLEKPSRTVTCPMSGKPLRMSDLTPVHFTPLDSSVDRVGLITRSERY VCAVTRDSLSNATPCAVLRPSGAVVTLECVEKLIRKDMVDPVTGDKLTDRDII VLQRGGT (SEQ ID NO:568),
YLYEREAILEYILHQKKEIARQMKAYEKQRGTRREEQKELQRAASQDHVRGF LE (SEQ ID NO:569),
FTAKALSGTSPDDVQPGPSVGPPSKDKDKVLPSFWIPSLTPEAKATKLEKPSR TVTCPMSGKPL (SEQ ID NO:570),
VHFTPLDSSVDRVGLITRSERYVCAVTRDSLSNATPCAVLRPSGAVVTLECVE KLI (SEQ ID NO:571), and/or
MSDLTPVHFTPLDSSVDRVGLITRSERYVCAVTRDSLSNATPCAVLRPSGAVV TLECVEKLIRKDM (SEQ ID NO:572).

Moreover, fragments and variants of these polypeptides (such as, for example, fragments as described herein, polypeptides at least 80%, 85%, 90%, 95%, 96%, 97%, 98%, or 99% identical to these polypeptides and polypeptides encoded by the polynucleotide which hybridizes, under stringent conditions, to the polynucleotide encoding these polypeptides) are encompassed by the invention. Antibodies that bind polypeptides of the invention are also encompassed by the invention. Polynucleotides encoding these polypeptides are also encompassed by the invention.

This gene is expressed primarily in human testis, and to a lesser extent in activated T-cells.

Polynucleotides and polypeptides of the invention are useful as reagents for differential identification of the tissue(s) or cell type(s) present in a biological sample and for diagnosis of diseases and conditions which include, but are not limited to,

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male reproductive disorders and in particular testicular cancer. Similarly, polypeptides and antibodies directed to these polypeptides are useful in providing immunological probes for differential identification of the tissue(s) or cell type(s). For a number of disorders of the above tissues or cells, particularly of the reproductive and immune systems, expression of this gene at significantly higher or lower levels may be routinely detected in certain tissues or cell types (e.g. testes, immune, cancerous and wounded tissues) or bodily fluids (e.g. lymph, serum, plasma, urine, synovial fluid and spinal fluid) or another tissue or cell sample taken from an individual having such a disorder, relative to the standard gene expression level, i.e., the expression level in healthy tissue or bodily fluid from an individual not having the disorder.

The tissue distribution in human testis indicates that the protein product of this gene is useful for the diagnosis and treatment of disorders of the male reproductive system, and in particular of testicular cancer. Furthermore, this gene is useful for the treatment and diagnosis of conditions concerning proper testicular function (e.g. endocrine function, sperm maturation), as well as cancer. Therefore, this gene product is useful in the treatment of male infertility and/or impotence. This gene product is also useful in assays designed to identify binding agents as such agents (antagonists) are useful as male contraceptive agents. Similarly, the protein is believed to by useful in the treatment and/or diagnosis of testicular cancer. The testes are also a site of active gene expression of transcripts that may be expressed, particularly at low levels, in other tissues of the body. Therefore, this gene product may be expressed in other specific tissues or organs where it may play related functional roles in other processes, such as hematopoiesis, inflammation, bone formation, and kidney function, to name a few possible target indications. Protein, as well as, antibodies directed against the protein may show utility as a tissue-specific marker and/or immunotherapy target for the above listed tissues.

Many polynucleotide sequences, such as EST sequences, are publicly available and accessible through sequence databases. Some of these sequences are related to SEQ ID NO:44 and may have been publicly available prior to conception of the present invention. Preferably, such related polynucleotides are specifically excluded from the scope of the present invention. To list every related sequence is

cumbersome. Accordingly, preferably excluded from the present invention are one or more polynucleotides comprising a nucleotide sequence described by the general formula of a-b, where a is any integer between 1 to 1010 of SEQ ID NO:44, b is an integer of 15 to 1024, where both a and b correspond to the positions of nucleotide residues shown in SEQ ID NO:44, and where b is greater than or equal to a + 14.

FEATURES OF PROTEIN ENCODED BY GENE NO: 35

The translation product of this gene shares sequence homology with Lpe5p of Saccharomyces cerevisiae, which is thought to be important in the metabolism of phospholipids. The gene encoding the disclosed cDNA is thought to reside on chromosome 8. Accordingly, polynucleotides related to this invention are useful as a marker in linkage analysis for chromosome 8.

This gene is expressed primarily in liver and brain.

Polynucleotides and polypeptides of the invention are useful as reagents for differential identification of the tissue(s) or cell type(s) present in a biological sample and for diagnosis of diseases and conditions which include, but are not limited to, metabolic disorders. Similarly, polypeptides and antibodies directed to these polypeptides are useful in providing immunological probes for differential identification of the tissue(s) or cell type(s). For a number of disorders of the above tissues or cells, particularly of the metabolic and nervous systems expression of this gene at significantly higher or lower levels may be routinely detected in certain tissues or cell types (e.g. liver, brain, cancerous and wounded tissues) or bodily fluids (e.g. lymph, serum, plasma, urine, synovial fluid and spinal fluid) or another tissue or cell sample taken from an individual having such a disorder, relative to the standard gene expression level, i.e., the expression level in healthy tissue or bodily fluid from an individual not having the disorder.

Predicted epitopes include those comprising a sequence shown in SEQ ID NO: 283 as residues: Pro-14 to Leu-20, Lys-28 to Asn-38, Arg-109 to Arg-114, Lys-119 to Asn-124, Glu-152 to Leu-157, or Pro-172 to Val-180.

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The tissue distribution in liver and brain, combined with the homology to Lpe5p of Saccharomyces cerevisiae indicates that the protein product of this gene is useful for the diagnosis and treatment of metabolic and nervous disorders. Additionally, the tissue distribution indicates that the protein product of this gene is useful for the detection and treatment of liver disorders and cancers (e.g. hepatoblastoma, jaundice, hepatitis, liver metabolic diseases and conditions that are attributable to the differentiation of hepatocyte progenitor cells). Protein, as well as, antibodies directed against the protein may show utility as a tumor marker and/or immunotherapy targets for the above listed tissues.

Many polynucleotide sequences, such as EST sequences, are publicly available and accessible through sequence databases. Some of these sequences are related to SEQ ID NO:45 and may have been publicly available prior to conception of the present invention. Preferably, such related polynucleotides are specifically excluded from the scope of the present invention. To list every related sequence is cumbersome. Accordingly, preferably excluded from the present invention are one or more polynucleotides comprising a nucleotide sequence described by the general formula of a-b, where a is any integer between 1 to 969 of SEQ ID NO:45, b is an integer of 15 to 983, where both a and b correspond to the positions of nucleotide residues shown in SEQ ID NO:45, and where b is greater than or equal to a + 14.

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FEATURES OF PROTEIN ENCODED BY GENE NO: 36

This gene shares sequence homology with the nuclear ribonucleoprotein U (HNRNP U), encoded by C. elegans (See Genbank Accession gi|1703576.).

In specific embodiments, polypeptides of the invention comprise, or alternatively consists of, an amino acid sequence selected from the group:
MDTSENRPENDVPEPPMPIADQVSNDDRPEGSVEDEEKKESSLPKSFKRKISV
VSATKGVPAGNSDTEGGQPGRKRRWGASTATTQKKPSISITTESLKSLIPDIKP
LAGQEAVVDLHADDSRISEDETERNGDDGTHDKGLKICRTVTQVVPAEGQE
NGQREEEEEEKEPEAEPPVPPQVSVEVALPPPAEHEVKKVTLGDTLTRRSISQ
QKSGVSITIDDPVRTAQVPSPPRGKISNIVHISNLVRPFTLGQLKELLGRTGTLV

EEAFWIDKIKSHCFVTYSTVEEAVATRTALHGVKWPQSNPKFLCADYAEQDE LDYHRGLLVDRPSETKTEEQGIPRPLHPPPPPPVQPPQHPRAEQREQERAVRE QWAERERERERRERTRSEREWDRDKvVREGPRSRSRSRXRRRKERAKSKEK KSEKKEKAQEEPPAKLLDDLFRKTKAAPCIYWLPLTDSQIVQKEAERAERAK EREKRRKEQEEEEQKEREKEAERERNRQLEREKRREHSRERDRERERERERD RGDRDRDRERDRERGRERDRRDTKRHSRSRSRSTPVRDRGGR (SEQ ID NO:573),

ENDVPEPPMPIADQVSNDDRPEGSVEDEEKKESSLPKSFKRKISVVSA (SEQ ID NO:574), VDLHADDSRISEDETERNGDDGTHDKGLKICRTVTQV (SEQ ID NO:575),

PQVSVEVALPPPAEHEVKKVTLGDTLTRRSISQQKSGVSITIDDPVRTAQVPSP P (SEQ ID NO:576),

LKELLGRTGTLVEEAFWIDKIKSHCFVTYSTVEEAVATRTALHGVKWPQSNP KFL (SEQ ID NO:577),

VDRPSETKTEEQGIPRPLHPPPPPPVQPPQHPRAEQREQERAVREQWAERERE (SEQ ID NO:578),

EWDRDKVREGPRSRSRSRXRRRKERAKSKEKKSEKKEKAQEEPPAKLLDDLF RKTKAAP (SEQ ID NO:579),LDVPLASRSPEFPLPLMTQSELPRCPPHPGAR (SEQ ID NO:581), LATLSISPIWSVLSL (SEQ ID NO:582), and

PLTDSQIVQKEAERAERAKEREKRRKEQEEEEQKEREKEAERERNRQLEREK RREHSRERDRER (SEQ ID NO:580). Moreover, fragments and variants of these polypeptides (such as, for example, fragments as described herein, polypeptides at least 80%, 85%, 90%, 95%, 96%, 97%, 98%, or 99% identical to these polypeptides and polypeptides encoded by the polynucleotide which hybridizes, under stringent conditions, to the polynucleotide encoding these polypeptides) are encompassed by the invention. Antibodies that bind polypeptides of the invention are also encompassed by the invention. Polynucleotides encoding these polypeptides are also encompassed by the invention.

An additional embodiment is the polynucleotides encoding these polypeptides. The gene encoding the disclosed cDNA is thought to reside on chromosome 14. Accordingly, polynucleotides related to this invention are useful as a marker in linkage analysis for chromosome 14.

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This gene is expressed primarily in epididymus, and to a lesser extent in testes.

Polynucleotides and polypeptides of the invention are useful as reagents for differential identification of the tissue(s) or cell type(s) present in a biological sample and for diagnosis of diseases and conditions which include, but are not limited to, diseases of the male reproductive system. Similarly, polypeptides and antibodies directed to these polypeptides are useful in providing immunological probes for differential identification of the tissue(s) or cell type(s). For a number of disorders of the above tissues or cells, particularly of the male reproductive system, expression of this gene at significantly higher or lower levels may be routinely detected in certain tissues or cell types (e.g. epididymus, testes, cancerous and wounded tissues) or bodily fluids (e.g. lymph, serum, plasma, urine, synovial fluid and spinal fluid) or another tissue or cell sample taken from an individual having such a disorder, relative to the standard gene expression level, i.e., the expression level in healthy tissue or bodily fluid from an individual not having the disorder.

The tissue distribution in epididymus and testes indicates that the protein product of this gene is useful for the diagnosis and treatment of male reproductive disorders. Furthermore, the protein product of this gene is useful for the treatment and diagnosis of conditions concerning proper reproductive and testicular function (e.g. endocrine function, sperm maturation), as well as cancer. Therefore, this gene product is useful in the treatment of male infertility and/or impotence. This gene product is also useful in assays designed to identify binding agents as such agents (antagonists) are useful as male contraceptive agents. Similarly, the protein is believed to by useful in the treatment and/or diagnosis of testicular cancer. The testes are also a site of active gene expression of transcripts that may be expressed, particularly at low levels, in other tissues of the body. Therefore, this gene product may be expressed in other specific tissues or organs where it may play related functional roles in other processes, such as hematopoiesis, inflammation, bone formation, and kidney function, to name a few possible target indications.

FEATURES OF PROTEIN ENCODED BY GENE NO: 37

This gene is expressed primarily in amygdala.

Polynucleotides and polypeptides of the invention are useful as reagents for differential identification of the tissue(s) or cell type(s) present in a biological sample and for diagnosis of diseases and conditions which include, but are not limited to, inflammatory diseases and reproductive disorders. Similarly, polypeptides and antibodies directed to these polypeptides are useful in providing immunological probes for differential identification of the tissue(s) or cell type(s). For a number of disorders of the above tissues or cells, particularly of the amygdala, expression of this gene at significantly higher or lower levels may be routinely detected in certain tissues or cell types (e.g. brain, cancerous and wounded tissues) or bodily fluids (e.g. lymph, serum, plasma, urine, synovial fluid and spinal fluid) or another tissue or cell sample taken from an individual having such a disorder, relative to the standard gene expression level, i.e., the expression level in healthy tissue or bodily fluid from an individual not having the disorder.

The tissue distribution in amygdala indicates that the protein product of this gene is useful for the diagnosis and treatment of inflammatory diseases and neural disorders. The amygdala processes sensory information and relays this to other areas of the brain including the endocrine and autonomic domains of the hypothalamus and the brain stem. Protein, as well as, antibodies directed against the protein may show utility as a tumor marker and/or immunotherapy targets for the above listed tissues.

Many polynucleotide sequences, such as EST sequences, are publicly available and accessible through sequence databases. Some of these sequences are related to SEQ ID NO:47 and may have been publicly available prior to conception of the present invention. Preferably, such related polynucleotides are specifically excluded from the scope of the present invention. To list every related sequence is cumbersome. Accordingly, preferably excluded from the present invention are one or more polynucleotides comprising a nucleotide sequence described by the general formula of a-b, where a is any integer between 1 to 826 of SEQ ID NO:47, b is an integer of 15 to 840, where both a and b correspond to the positions of nucleotide residues shown in SEQ ID NO:47, and where b is greater than or equal to a + 14.

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FEATURES OF PROTEIN ENCODED BY GENE NO: 38

This gene shares sequence homology with human opsonin protein P35 fragment. (See Genbank Accession No. R94181.) The opsonin protein activates the phagocytosis of pathogenic microbes by phagocytic cells which indicates that the protein product of this gene may be useful in the treatment and/or prevention of a variety of immune conditions, particularly bacterial infections and antigen presentation.

In specific embodiments, polypeptides of the invention comprise, or alternatively consists of, an amino acid sequence selected from the group: GCDSCPPHLPREAFAQDTQAEGECSSRAERADMCPDAPPSQEVPEGPGAAP (SEQ ID NO:583), RGWLPSSCLSCALRVCPDSSSTQAMGMLLAFWLPGASWQEAARGQYSEDED TDTDEYKEAKASINPVTGRVEEKPPNPMEGMTEEQKEHEA (SEQ ID NO:584), and/or TQAMGMLLAFWLPGASWQEAARGQYSE (SEQ ID NO:585). Moreover, fragments and variants of these polypeptides (such as, for example, fragments as described herein, polypeptides at least 80%, 85%, 90%, 95%, 96%, 97%, 98%, or 99% identical to these polypeptides and polypeptides encoded by the polynucleotide which hybridizes, under stringent conditions, to the polynucleotide encoding these polypeptides) are encompassed by the invention. Antibodies that bind polypeptides of the invention are also encompassed by the invention. Polynucleotides encoding these polypeptides are also encompassed by the invention.

This gene is expressed in immune-related tissues such as thymus, macrophage, and T cells.

Polynucleotides and polypeptides of the invention are useful as reagents for differential identification of the tissue(s) or cell type(s) present in a biological sample and for diagnosis of diseases and conditions which include, but are not limited to, immune disorders and infectious diseases. Similarly, polypeptides and antibodies directed to these polypeptides are useful in providing immunological probes for differential identification of the tissue(s) or cell type(s). For a number of disorders of the above tissues or cells, particularly of the immune system, expression of this gene

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at significantly higher or lower levels may be routinely detected in certain tissues or cell types (e.g., immune, hematopoietic, and cancerous and wounded tissues) or bodily fluids (e.g., lymph, serum, plasma, urine, synovial fluid and spinal fluid) or another tissue or cell sample taken from an individual having such a disorder, relative to the standard gene expression level, i.e., the expression level in healthy tissue or bodily fluid from an individual not having the disorder.

Predicted epitopes include those comprising a sequence shown in SEQ ID NO: 286 as residues: Lys-9 to Arg-14, or Met-38 to Asp-51.

The tissue distribution in immune tissues, particularly macrophages, combined with the homology to a conserved human opsonin protein indicates that the protein product of this gene is useful for diagnosis and treatment of immune disorders, as well as the treatment and/or diagnosis of infectious disease. Moreover, the gene product may be involved in the regulation of cytokine production, antigen presentation, or other processes that may also suggest a usefulness in the treatment of cancer (e.g. by boosting immune responses). Since the gene is expressed in cells of lymphoid origin, the natural gene product may be involved in immune functions. Therefore it may be also used as an agent for immunological disorders including arthritis, asthma, immunodeficiency diseases such as AIDS, leukemia, rheumatoid arthritis, granulomatous disease, inflammatory bowel disease, sepsis, acne, neutropenia, neutrophilia, psoriasis, hypersensitivities, such as T-cell mediated cytotoxicity; immune reactions to transplanted organs and tissues, such as host-versus-graft and graft-versus-host diseases, or autoimmunity disorders, such as autoimmune infertility, lens tissue injury, demyelination, systemic lupus erythematosis, drug induced hemolytic anemia, rheumatoid arthritis, Sjogren's disease, scleroderma and tissues. In addition, this gene product may have commercial utility in the expansion of stem cells and committed progenitors of various blood lineages, and in the differentiation and/or proliferation of various cell types. Protein, as well as, antibodies directed against the protein may show utility as a tumor marker and/or immunotherapy targets for the above listed tissues.

Many polynucleotide sequences, such as EST sequences, are publicly available and accessible through sequence databases. Some of these sequences are related to SEQ ID NO:48 and may have been publicly available prior to conception of

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the present invention. Preferably, such related polynucleotides are specifically excluded from the scope of the present invention. To list every related sequence is cumbersome. Accordingly, preferably excluded from the present invention are one or more polynucleotides comprising a nucleotide sequence described by the general formula of a-b, where a is any integer between 1 to 2418 of SEQ ID NO:48, b is an integer of 15 to 2432, where both a and b correspond to the positions of nucleotide residues shown in SEQ ID NO:48, and where b is greater than or equal to a + 14.

FEATURES OF PROTEIN ENCODED BY GENE NO: 39

The translation product of this gene shares sequence homology with alpha-2 type I collagen which is thought to be important in tissue repair. (See, e.g., Genbank Accession No. 211607.)

In specific embodiments, polypeptides of the invention comprise, or alternatively consists of, an amino acid sequence selected from the group: PQLPSCGRPWPGTASVFQSHTQGPREDPDPCRAQGSAGTHCPISLSPPRQ (SEQ ID NO:586),

KTHPRALWSAGPSCALCPGGSGXTSPPQGAPRGIXWDRCPQIQVLEGQRVRF PSQPQHPSHLAPRGGCGWRPDSRPLLPTPSGLSSFFPLDA QCWPWRTVSWR (SEQ ID NO:587),

AGAPGQQARLQYLLSFQGEGAPHEXGATGEGGDGAWEACXCXRCLLNWQA GGWGLQLSLMWLHRGPLRPPGVRWTPWAFLEACSWGPALSLLGSGHSLPGT HEQAAWSRGCGQHGQSPTQKCKSSKEPLAQAPPWDSPAAPPHQGFADVLER PTLEPFGVLAPPVPSALVEAAXQVLLREPQGGFXGTAAHRSRCWKGSG (SEQ ID NO:588),

MQLLFLLPHPSPQLHASLPHSAALPCPRGESLTTASPAGAAGRXDAVPRCRH QAGRGWVPRGPCERGGGDRGKPRAVAWDXGSLRWAVWSARAGQGRSSEP APLASRRGYSTCCLSRGKGLPMRXGRRGRGVMVPGKPACAXGAC (SEQ ID NO:589), QHPSHLAPRGGCGWRPDSRPLLPTPSGLSSFFPL (SEQ ID NO:590), GVRWTPWAFLEACSWGPALSLLGSGHSLPG (SEQ ID NO:591), WDSPAAPPHQGFADVLERPTLEPFGVLA (SEQ ID NO:592), and/or

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RSSEPAPLASRRGYSTCCLSRGKGL PMR (SEQ ID NO:593). Moreover, fragments and variants of these polypeptides (such as, for example, fragments as described herein, polypeptides at least 80%, 85%, 90%, 95%, 96%, 97%, 98%, or 99% identical to these polypeptides and polypeptides encoded by the polynucleotide which hybridizes, under stringent conditions, to the polynucleotide encoding these polypeptides) are encompassed by the invention. Antibodies that bind polypeptides of the invention are also encompassed by the invention. Polynucleotides encoding these polypeptides are also encompassed by the invention.

This gene is expressed primarily in the brain, and to a lesser extent, in the kidney and thymus

Polynucleotides and polypeptides of the invention are useful as reagents for differential identification of the tissue(s) or cell type(s) present in a biological sample and for diagnosis of diseases and conditions which include, but are not limited to, brain, kidney, endocrine, hematopoietic, and immune disorders. Similarly, polypeptides and antibodies directed to these polypeptides are useful in providing immunological probes for differential identification of the tissue(s) or cell type(s). For a number of disorders of the above tissues or cells, particularly of the brain, kidney, and immune disorders, expression of this gene at significantly higher or lower levels may be routinely detected in certain tissues or cell types (e.g., neural, urogenital, renal, immune, hematopoietic, and cancerous and wounded tissues) or bodily fluids (e.g., lymph, serum, plasma, urine, synovial fluid and spinal fluid) or another tissue or cell sample taken from an individual having such a disorder, relative to the standard gene expression level, i.e., the expression level in healthy tissue or bodily fluid from an individual not having the disorder.

The tissue distribution in brain and thymus, combined with the homology to an alpha-2 type I collagen protein indicates that the protein product of this gene is useful for the diagnosis and treatment of tissue repair, and brain, kidney, immune disorders. Moreover, this protein may also be important in the diagnosis or treatment of various autoimmune disorders such as rheumatoid arthritis, lupus, scleroderma, and dermatomyositis as well as dwarfism, spinal deformation, and specific joint abnormalities as well as chondrodysplasias i.e. spondyloepiphyseal dysplasia congenita, familial osteoarthritis, Atelosteogenesis type II, metaphyseal

chondrodysplasia type Schmid. Protein, as well as, antibodies directed against the protein may show utility as a tumor marker and/or immunotherapy targets for the above listed tissues.

Many polynucleotide sequences, such as EST sequences, are publicly available and accessible through sequence databases. Some of these sequences are related to SEQ ID NO:49 and may have been publicly available prior to conception of the present invention. Preferably, such related polynucleotides are specifically excluded from the scope of the present invention. To list every related sequence is cumbersome. Accordingly, preferably excluded from the present invention are one or more polynucleotides comprising a nucleotide sequence described by the general formula of a-b, where a is any integer between 1 to 1728 of SEQ ID NO:49, b is an integer of 15 to 1742, where both a and b correspond to the positions of nucleotide residues shown in SEQ ID NO:49, and where b is greater than or equal to a + 14.

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FEATURES OF PROTEIN ENCODED BY GENE NO: 40

The translation product of this gene shares sequence homology with mini-collagen which is thought to be important in tissue repair and tumor metastasis, and potentially in cellular migration, attachment, and/or chemotaxis. (See Genbank Accession No. gnl|PID|d1006976.)

In specific embodiments, polypeptides of the invention comprise, or alternatively consists of, the following amino acid sequence: PGFRGPSGSLGCSFFPRSLGRVLPPGCQRPGAHADSSPPPTP (SEQ ID NO:594). Moreover, fragments and variants of this polypeptide (such as, for example, fragments as described herein, polypeptides at least 80%, 85%, 90%, 95%, 96%, 97%, 98%, or 99% identical to these polypeptides and polypeptides encoded by the polynucleotide which hybridize, under stringent conditions, to the polynucleotide encoding this polypeptide are encompassed by the invention. Antibodies that bind polypeptides of the invention are also encompassed by the invention. Polynucleotides encoding this polypeptide are also encompassed by the invention.

The gene encoding the disclosed cDNA is believed to reside on chromosome 16. Accordingly, polynucleotides related to this invention are useful as a marker in linkage analysis for chromosome 16.

This gene is expressed in ovarian cancer, and to a lesser extent, in dendritic cells and smooth muscle.

Polynucleotides and polypeptides of the invention are useful as reagents for differential identification of the tissue(s) or cell type(s) present in a biological sample and for diagnosis of diseases and conditions which include, but are not limited to, tumor metastasis, tissue repair, integumentary, reproductive, and/or immune disorders, particularly cancers. Similarly, polypeptides and antibodies directed to these polypeptides are useful in providing immunological probes for differential identification of the tissue(s) or cell type(s). For a number of disorders of the above tissues or cells, particularly of the tumor metastasis and tissue repair, expression of this gene at significantly higher or lower levels may be routinely detected in certain tissues or cell types (e.g., integumentary, immune, hematopoietic, reproductive, ovarian, and cancerous and wounded tissues) or bodily fluids (e.g., lymph, serum, plasma, urine, synovial fluid and spinal fluid) or another tissue or cell sample taken from an individual having such a disorder, relative to the standard gene expression level, i.e., the expression level in healthy tissue or bodily fluid from an individual not having the disorder.

Predicted epitopes include those comprising a sequence shown in SEQ ID NO: 288 as residues: Asn-2 to His-11.

The tissue distribution in dendritic cells, combined with the homology to the mini-collagen gene indicates that the protein product of this gene is useful for diagnosis and treatment of tumor metastasis and tissue repair. Alternatively, this protein may also be important in the diagnosis or treatment of various autoimmune disorders such as rheumatoid arthritis, lupus, scleroderma, and dermatomyositis as well as dwarfism, spinal deformation, and specific joint abnormalities as well as chondrodysplasias i.e. spondyloepiphyseal dysplasia congenita, familial osteoarthritis, Atelosteogenesis type II, metaphyseal chondrodysplasia type Schmid. Protein, as well as, antibodies directed against the protein may show utility as a tumor marker and/or immunotherapy targets for the above listed tissues.

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Many polynucleotide sequences, such as EST sequences, are publicly available and accessible through sequence databases. Some of these sequences are related to SEQ ID NO:50 and may have been publicly available prior to conception of the present invention. Preferably, such related polynucleotides are specifically excluded from the scope of the present invention. To list every related sequence is cumbersome. Accordingly, preferably excluded from the present invention are one or more polynucleotides comprising a nucleotide sequence described by the general formula of a-b, where a is any integer between 1 to 1473 of SEQ ID NO:50, b is an integer of 15 to 1487, where both a and b correspond to the positions of nucleotide residues shown in SEQ ID NO:50, and where b is greater than or equal to a + 14.

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FEATURES OF PROTEIN ENCODED BY GENE NO: 41

This gene shares sequence homology with the HIV TAT protein. (See Genbank Accession No. 328416.)

In specific embodiments, polypeptides of the invention comprise, or alternatively consists of, an amino acid sequence selected from the group: EDLKKPDPASLRAASCGEGKKRKACKNCTCGLAEELEKEKSREQMSSQPKSA CGNCYLGDAFRCASCPYLGMPAFKPGEKVLLS (SEQ ID NO:595); EDLKKPDPASLRAASCGEGKKRKACKNCTCGLAEELEKEKSREQMSSQPKSA CGNCYLGDAFRCASCPYLGMPAFKPGEKVLLSDSNLHD (SEQ ID NO:596); CGNCYLGDAFRCASCPYLGMPAFKPGEKVLLSDS (SEQ ID NO:597); SCGEGKKRKACKNCTCGLAEELEKE (SEQ ID NO:598), SQPKSACGNCYLGDAFRCASC (SEQ ID NO:599); CCCVSKDQGIMGPGFR (SEQ ID NO:601), HSVTELQTPALSLISAMLPPSCLSELLVYSILCDTSQVAHNLLRAPEDSLTGCC DDIQCPSAPFHPQPHLTVALHLCPVVIYVNLQVLNLLHILTYLEILHVL (SEQ ID NO:602), LLVYSILCDTSQVAHNLLRAPEDS (SEQ ID NO:603), LTVALHLCPVVIYVNLQVLNLLHILT (SEQ ID NO:604), and/or REAGQNSERQYVSLSRDP (SEQ ID NO:600). Moreover, fragments and variants of these polypeptides (such as, for example, fragments as described herein,

polypeptides at least 80%, 85%, 90%, 95%, 96%, 97%, 98%, or 99% identical to these polypeptides and polypeptides encoded by the polynucleotide which hybridizes, under stringent conditions, to the polynucleotide encoding these polypeptides) are encompassed by the invention. Antibodies that bind polypeptides of the invention are also encompassed by the invention. Polynucleotides encoding these polypeptides are also encompassed by the invention.

This gene is expressed primarily in the infant brain, and to a lesser extent, in the breast and testes.

Polynucleotides and polypeptides of the invention are useful as reagents for differential identification of the tissue(s) or cell type(s) present in a biological sample and for diagnosis of diseases and conditions which include, but are not limited to, neural, developmental, reproductive, brain, testes and breast disorders. Similarly, polypeptides and antibodies directed to these polypeptides are useful in providing immunological probes for differential identification of the tissue(s) or cell type(s). For a number of disorders of the above tissues or cells, particularly of the brain, testes and breast disorders, expression of this gene at significantly higher or lower levels may be routinely detected in certain tissues or cell types (e.g., neural, developmental, reproductive, testicular, breast, and cancerous and wounded tissues) or bodily fluids (e.g., seminal fluid, amniotic fluid, lymph, serum, plasma, urine, synovial fluid and spinal fluid) or another tissue or cell sample taken from an individual having such a disorder, relative to the standard gene expression level, i.e., the expression level in healthy tissue or bodily fluid from an individual not having the disorder.

Predicted epitopes include those comprising a sequence shown in SEQ ID NO: 289 as residues: Pro-7 to Val-15.

The tissue distribution in infant brain tissue indicates that the protein product of this gene is useful for diagnosis and treatment of neural and other related disorders. Similarly the protein product of this gene is useful for the detection/treatment of neurodegenerative disease states, behavioral disorders, or inflammatory conditions such as Alzheimer's Disease, Parkinson's Disease, Huntington's Disease, Tourette's Syndrome, meningitis, encephalitis, demyelinating diseases, peripheral neuropathies, neoplasia, trauma, congenital malformations, spinal cord injuries, ischemia and infarction, aneurysms, hemorrhages, schizophrenia, mania, dementia, paranoia,

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obsessive compulsive disorder, panic disorder, learning disabilities, ALS, psychoses, autism, and altered behaviors, including disorders in feeding, sleep patterns, balance, and perception. In addition, elevated expression of this gene product in regions of the brain indicates that it plays a role in normal neural function. Potentially, this gene product is involved in synapse formation, neurotransmission, learning, cognition, homeostasis, or neuronal differentiation or survival. Moreover, the gene or gene product may also play a role in the treatment and/or detection of developmental disorders associated with the developing embryo, sexually-linked disorders, or disorders of the cardiovascular or reproductive system. Protein, as well as, antibodies directed against the protein may show utility as a tumor marker and/or immunotherapy targets for the above listed tissues.

Many polynucleotide sequences, such as EST sequences, are publicly available and accessible through sequence databases. Some of these sequences are related to SEQ ID NO:51 and may have been publicly available prior to conception of the present invention. Preferably, such related polynucleotides are specifically excluded from the scope of the present invention. To list every related sequence is cumbersome. Accordingly, preferably excluded from the present invention are one or more polynucleotides comprising a nucleotide sequence described by the general formula of a-b, where a is any integer between 1 to 1314 of SEQ ID NO:51, b is an integer of 15 to 1328, where both a and b correspond to the positions of nucleotide residues shown in SEQ ID NO:51, and where b is greater than or equal to a + 14.

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FEATURES OF PROTEIN ENCODED BY GENE NO: 42

In specific embodiments, polypeptides of the invention comprise, or alternatively consists of, the following amino acid sequence: FFNALYVFRKPQAIFDSEKENKRKNPTKYNNPLRYIYFKVKLIFQFIPLANYKI K (SEQ ID NO:605). Moreover, fragments and variants of this polypeptide (such as, for example, fragments as described herein, polypeptides at least 80%, 85%, 90%, 95%, 96%, 97%, 98%, or 99% identical to these polypeptides and polypeptides encoded by the polynucleotide which hybridize, under stringent conditions, to the

polynucleotide encoding this polypeptide are encompassed by the invention. Antibodies that bind polypeptides of the invention are also encompassed by the invention. Polynucleotides encoding this polypeptide are also encompassed by the invention.

The gene encoding the disclosed cDNA is believed to reside on chromosome 3. Accordingly, polynucleotides related to this invention are useful as a marker in linkage analysis for chromosome 3.

This gene is expressed primarily in the infant brain, human cerebellum, and to a lesser extent, in medulloblastoma.

Polynucleotides and polypeptides of the invention are useful as reagents for differential identification of the tissue(s) or cell type(s) present in a biological sample and for diagnosis of diseases and conditions which include, but are not limited to, brain related disorders, such as neurodegenerative conditions, medulloblastoma, and other cancers or proliferative conditions. Similarly, polypeptides and antibodies directed to these polypeptides are useful in providing immunological probes for differential identification of the tissue(s) or cell type(s). For a number of disorders of the above tissues or cells, particularly of the brain related disorders and brain cancers, including medulloblastoma, expression of this gene at significantly higher or lower levels may be routinely detected in certain tissues or cell types (e.g., neural, developmental, and cancerous and wounded tissues) or bodily fluids (e.g., lymph, amniotic fluid, serum, plasma, urine, synovial fluid and spinal fluid) or another tissue or cell sample taken from an individual having such a disorder, relative to the standard gene expression level, i.e., the expression level in healthy tissue or bodily fluid from an individual not having the disorder.

Predicted epitopes include those comprising a sequence shown in SEQ ID NO: 290 as residues: Thr-41 to Glu-47.

The tissue distribution in infant brain and medulloblastoma indicates that the protein product of this gene is useful for diagnosis and treatment of human brain related disorders, brain cancers, and medulloblastoma. Similarly, the protein product of this gene is useful for the detection/treatment of neurodegenerative disease states, behavioral disorders, or inflammatory conditions such as Alzheimer's Disease, Parkinson's Disease, Huntington's Disease, Tourette's Syndrome, meningitis,

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encephalitis, demyelinating diseases, peripheral neuropathies, neoplasia, trauma, congenital malformations, spinal cord injuries, ischemia and infarction, aneurysms, hemorrhages, schizophrenia, mania, dementia, paranoia, obsessive compulsive disorder, panic disorder, learning disabilities, ALS, psychoses, autism, and altered behaviors, including disorders in feeding, sleep patterns, balance, and perception. In addition, elevated expression of this gene product in regions of the brain indicates that it plays a role in normal neural function. Potentially, this gene product is involved in synapse formation, neurotransmission, learning, cognition, homeostasis, or neuronal differentiation or survival. Moreover, the gene or gene product may also play a role in the treatment and/or detection of developmental disorders associated with the developing embryo, sexually-linked disorders, or disorders of the cardiovascular system. Protein, as well as, antibodies directed against the protein may show utility as a tumor marker and/or immunotherapy targets for the above listed tissues.

Many polynucleotide sequences, such as EST sequences, are publicly available and accessible through sequence databases. Some of these sequences are related to SEQ ID NO:52 and may have been publicly available prior to conception of the present invention. Preferably, such related polynucleotides are specifically excluded from the scope of the present invention. To list every related sequence is cumbersome. Accordingly, preferably excluded from the present invention are one or more polynucleotides comprising a nucleotide sequence described by the general formula of a-b, where a is any integer between 1 to 1842 of SEQ ID NO:52, b is an integer of 15 to 1856, where both a and b correspond to the positions of nucleotide residues shown in SEQ ID NO:52, and where b is greater than or equal to a + 14.

FEATURES OF PROTEIN ENCODED BY GENE NO: 43

The translation product of this gene shares sequence homology with a phosphotyrosine-independent ligand for the lck SH2 domain which is thought to be important in signal transduction related to phosphotyrosine-independent ligand for the lck SH2 domain, which may implicate this protein as playing an essential role in

regulating key cellular processes such as cellular division, and potentially in male fertility. (See Genbank Accession No. gi|1184951.)

In specific embodiments, polypeptides of the invention comprise, or alternatively consists of, an amino acid sequence selected from the group: ESSGQARTLADPGPGWPRQQGMCFGSLTGLSTTPHGFLTVSAEADPRLIESLS QMLSMGFSDEGGWLTRLLQTKNYDIGAALDTIQYSKH (SEQ ID NO:606), YSMVYIYHIFFIHSLLDGQLGWFHIFAIVSCAAPDIIFNSFAFSTYISKSCSFYLQ NVSCIHSSLSIFNLFQCPIISCMEECNNWLTGLFLHFKIKRCDR (SEQ ID NO:607), LSPSPRCCPWASLMKAAGSPGSCRPRTMTSERLWTPSSIQSIPRRCDHFCPPLL RAPLLSHSCVKLA (SEQ ID NO:608), GWPRQQGMCFGSLTGLSTTPHGFLTVSAEADPRL (SEQ ID NO:609), LGWFHIFAIVSCAAPDIIFNSFAFSTYISKSCS (SEQ ID NO:610), SLSIFNLFQCPIISCMEECNNWLTG (SEQ ID NO:611), and/or LMKAAGSPGSCRPRTMTSERLWTPSSIQSI (SEQ ID NO:612). Moreover, fragments and variants of these polypeptides (such as, for example, fragments as described herein, polypeptides at least 80%, 85%, 90%, 95%, 96%, 97%, 98%, or 99% identical to these polypeptides and polypeptides encoded by the polynucleotide which hybridizes, under stringent conditions, to the polynucleotide encoding these polypeptides) are encompassed by the invention. Antibodies that bind polypeptides of the invention are also encompassed by the invention. Polynucleotides encoding these polypeptides are also encompassed by the invention.

It is likely that this gene is a new member of a family of phosphotyrosine-independent ligands for the lck SH2 domains.

This gene is expressed primarily in the placenta, and to a lesser extent, in endothelial cells and neutrophils.

Polynucleotides and polypeptides of the invention are useful as reagents for differential identification of the tissue(s) or cell type(s) present in a biological sample and for diagnosis of diseases and conditions which include, but are not limited to, reproductive, cardiovascular, immune, and infectious diseases. Similarly, polypeptides and antibodies directed to these polypeptides are useful in providing immunological probes for differential identification of the tissue(s) or cell type(s).

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For a number of disorders of the above tissues or cells, particularly of the cardiovascular, reproductive, and immune system, and infectious diseases, expression of this gene at significantly higher or lower levels may be routinely detected in certain tissues or cell types (e.g., reproductive, cardiovascular, immune, hematopoietic, and cancerous and wounded tissues) or bodily fluids (e.g., lymph, amniotic fluid, seminal fluid, serum, plasma, urine, synovial fluid and spinal fluid) or another tissue or cell sample taken from an individual having such a disorder, relative to the standard gene expression level, i.e., the expression level in healthy tissue or bodily fluid from an individual not having the disorder.

Predicted epitopes include those comprising a sequence shown in SEQ ID NO: 291 as residues: Ile-93 to Arg-98.

The tissue distribution in placenta and endothelial tissues, combined with the homology to a phosphotyrosine-independent ligand for the lck SH2 domain indicates that the protein product of this gene is useful for diagnosis and treatment of cardiovascular, reproductive, and immune system diseases, as well as infectious diseases. Moreover, the polypeptide of this gene may be able to modulate T or B cell development and/or T or B cell activation (e.g. by modulation of Lck activity). It may also be capable of modulating degradation of cellular proteins (e.g. cell cycle regulatory proteins stimulating expression of cell cycle dependent kinase inhibitors and arresting cell cycle progression at specific boundaries to thereby modulate cell proliferation). p62 acts to boost B cell response and may be used to treat disorders where this is beneficial, e.g. infections by pathogenic microorganisms, e.g. bacteria, viruses and protozoans. p62 can be used to expand T cell populations for treating infectious diseases or cancer, e.g. the resulting cells may be transduced to render them resistant to HIV infection. Inhibitors of p62 can be used to reduce B or T cell responses and may be used to treat a variety of autoimmune diseases, e.g. diabetes mellitus, arthritis, multiple sclerosis allergic reactions, Crohn's diseases etc. Protein, as well as, antibodies directed against the protein may show utility as a tumor marker and/or immunotherapy targets for the above listed tissues.

Many polynucleotide sequences, such as EST sequences, are publicly available and accessible through sequence databases. Some of these sequences are related to SEQ ID NO:53 and may have been publicly available prior to conception of

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the present invention. Preferably, such related polynucleotides are specifically excluded from the scope of the present invention. To list every related sequence is cumbersome. Accordingly, preferably excluded from the present invention are one or more polynucleotides comprising a nucleotide sequence described by the general formula of a-b, where a is any integer between 1 to 1544 of SEQ ID NO:53, b is an integer of 15 to 1558, where both a and b correspond to the positions of nucleotide residues shown in SEQ ID NO:53, and where b is greater than or equal to a + 14.

FEATURES OF PROTEIN ENCODED BY GENE NO: 44

In specific embodiments, polypeptides of the invention comprise, or alternatively consists of, the following amino acid sequences: SSSSPRRPRELLGSLKTPLVRPHSAPLDLPGSFCXHTADPMGALHTRFWGRQT WIHRKLRLHGTSRLASKXGIQFLRNPSKTHTPRDAAFRDPGQTPDPQSLQAPS PSKCSAPNRATSVWSLKPRLLYKHRPSSDKTPPPGRQAPLLFFSAG (SEQ ID NO:613), and/or FLRNPSKTHTPRDAAFRDPGQTPDPQSLQA (SEQ ID NO:614). Moreover, fragments and variants of these polypeptides (such as, for example, fragments as described herein, polypeptides at least 80%, 85%, 90%, 95%, 96%, 97%, 98%, or 99% identical to these polypeptides and polypeptides encoded by the polynucleotide which hybridizes, under stringent conditions, to the polynucleotide encoding these polypeptides) are encompassed by the invention. Antibodies that bind polypeptides of the invention are also encompassed by the invention. Polynucleotides encoding these polypeptides are also encompassed by the invention.

This gene is expressed primarily in the fetal brain, cerebellum, and to a lesser extent, in the placenta.

Polynucleotides and polypeptides of the invention are useful as reagents for differential identification of the tissue(s) or cell type(s) present in a biological sample and for diagnosis of diseases and conditions which include, but are not limited to, neural, developmental, or reproductive disorders, particularly cancers. Similarly, polypeptides and antibodies directed to these polypeptides are useful in providing

immunological probes for differential identification of the tissue(s) or cell type(s). For a number of disorders of the above tissues or cells, particularly of the neuronal cell related disorders, expression of this gene at significantly higher or lower levels may be routinely detected in certain tissues or cell types (e.g., neural, reproductive, vascular, and cancerous and wounded tissues) or bodily fluids (e.g., lymph, amniotic fluid, serum, plasma, urine, synovial fluid and spinal fluid) or another tissue or cell sample taken from an individual having such a disorder, relative to the standard gene expression level, i.e., the expression level in healthy tissue or bodily fluid from an individual not having the disorder.

Predicted epitopes include those comprising a sequence shown in SEQ ID NO: 292 as residues: Thr-20 to Gly-28.

The tissue distribution in fetal brain, combined with the homology to proline-rich protein genes indicates that the protein product of this gene is useful for diagnosis and treatment of neuronal cell related disorders. Similarly, the protein product of this gene is useful for the detection/treatment of neurodegenerative disease states, behavioral disorders, or inflammatory conditions such as Alzheimer's Disease, Parkinson's Disease, Huntington's Disease, Tourette's Syndrome, meningitis, encephalitis, demyelinating diseases, peripheral neuropathies, neoplasia, trauma, congenital malformations, spinal cord injuries, ischemia and infarction, aneurysms, hemorrhages, schizophrenia, mania, dementia, paranoia, obsessive compulsive disorder, panic disorder, learning disabilities, ALS, psychoses, autism, and altered behaviors, including disorders in feeding, sleep patterns, balance, and perception. In addition, elevated expression of this gene product in regions of the brain indicates that it plays a role in normal neural function. Potentially, this gene product is involved in synapse formation, neurotransmission, learning, cognition, homeostasis, or neuronal differentiation or survival. Moreover, the gene or gene product may also play a role in the treatment and/or detection of developmental disorders associated with the developing embryo, sexually-linked disorders, or disorders of the cardiovascular system. Moreover, expression within fetal tissue and other cellular sources marked by proliferating cells indicates that this protein may play a role in the regulation of cellular division, and may show utility in the diagnosis and treatment of cancer and other proliferative disorders. Similarly, developmental tissues rely on decisions

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involving cell differentiation and/or apoptosis in pattern formation. Thus this protein may also be involved in apoptosis or tissue differentiation and could again be useful in cancer therapy. Protein, as well as, antibodies directed against the protein may show utility as a tumor marker and/or immunotherapy targets for the above listed tissues.

Many polynucleotide sequences, such as EST sequences, are publicly available and accessible through sequence databases. Some of these sequences are related to SEQ ID NO:54 and may have been publicly available prior to conception of the present invention. Preferably, such related polynucleotides are specifically excluded from the scope of the present invention. To list every related sequence is cumbersome. Accordingly, preferably excluded from the present invention are one or more polynucleotides comprising a nucleotide sequence described by the general formula of a-b, where a is any integer between 1 to 934 of SEQ ID NO:54, b is an integer of 15 to 948, where both a and b correspond to the positions of nucleotide residues shown in SEQ ID NO:54, and where b is greater than or equal to a + 14.

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FEATURES OF PROTEIN ENCODED BY GENE NO: 45

The translation product of this gene shares sequence homology with precerebellin of human, which is thought to be important in synaptic physiology. (See Genbank Accession No. gi|180251.) The cerebellum contains a hexadecapeptide, termed cerebellin, that is conserved in sequence from human to chicken. Three independent, overlapping cDNA genes have been isolated from a human cerebellum cDNA library that encode the cerebellin sequence. The longest gene codes for a protein of 193 amino acids that we term precerebellin. This protein has a significant similarity (31.3% identity, 52.2% similarity) to the globular (non-collagen-like) region of the B chain of human complement component C1q. The region of relatedness extends over approximately 145 amino acids located in the carboxyl terminus of both proteins. Unlike C1q B chain, no collagen-like motifs are present in the amino-terminal regions of precerebellin. The amino terminus of precerebellin contains three possible N-linked glycosylation sites. Although

hydrophobic amino acids are clustered at the amino terminus, they do not conform to the classical signal-peptide motif, and no other obvious membrane-spanning domains are predicted from the cDNA sequence. The cDNA predicts that the cerebellin peptide is flanked by Val-Arg and Glu-Pro residues. Therefore, cerebellin is not liberated from precerebellin by the classical dibasic amino acid proteolytic-cleavage mechanism seen in many neuropeptide precursors. In Northern (RNA) blots, precerebellin transcripts, with four distinct sizes (1.8, 2.3, 2.7, and 3.0 kilobases), are abundant in cerebellum. These transcripts are present at either very low or undetectable levels in other brain areas and extraneural structures. A similar pattern of cerebellin precursor transcripts are seen in rat, mouse, and human cerebellum. Furthermore, a partial genomic fragment from mouse shows the same bands in Northern blots as the human cDNA gene. During rat development, precerebellin transcripts mirror the level of cerebellin peptide. Low levels of precerebellin mRNA are seen at birth. Levels increase modestly from postpartum day 1 to 8, then increase more dramatically between day 5 and 15, and eventually reach peak values between day 21 and 56. It has been observed that cerebellin-like immunoreactivity is associated with Purkinje cell postsynaptic structures. Thus, it is likely that this gene also have synaptic activity. Northern analysis showed a brain-specific 2.4kb message. This is consistent with the current insert size we have, suggesting our gene is full-length and is brain-specific.

In specific embodiments, polypeptides of the invention comprise, or alternatively consists of, an amino acid sequence selected from the group: QEGSEPVLLEGECLVVCEPGRAAAGGPGGAALGEAPPGRVAFXAVRSHHHEP AGETGNGTSGAIYFDQVLVNEGGGFDRASGSFVAPVRGVYSFRFHVVKVYN RQTVQVSLMLNTWPVISAFANDPDVTREAATSSVLLPLDPGDRVSLRLRRGX STGW (SEQ ID NO:615), GETGNGTSGAIYFDQVLVNEGGGFDRASGSFVAPV (SEQ ID NO:616), NDPDVTREAATSSVLLPLDPGDRVS (SEQ ID NO:617), FHVVKVYNRQT (SEQ ID NO:618), IYFDQVLVN (SEQ ID NO:619), ESRERSGNRRGAEDRGTCGLQSPSA (SEQ ID NO:620), EMPQFYFFLKLGCLAQVPMQRGGIGARGSXXPAXAVXGAREGRRKLSGAGF LCLKDLGPSEREDEEARET (SEQ ID NO:621), MPQFYFFLKLGCLAQVPMQRGGIGARG (SEQ ID NO:622),

QATCSASGSPGQFGGCTPSPHGTGSCRHPGQGLRRSQRPGQSHRPRSPGPGRS
RWPHWCHCRFPLLAHGGGFGPQQMPLAQGVPLPGLLPRAPLQQLGQAHRPP
GTPPPAGRALTPPGPTRPPGPEAPEPRAARDCVGDLVASVAWLPTWLRGSAT
HKCPGLLPLFCFRSSPWILTAGTLIVCPL (SEQ ID NO:623),
GCTPSPHGTGSCRHPGQGLRRSQRP (SEQ ID NO:624),
SRWPHWCHCRFPLLAHGGGFGPQQMP (SEQ ID NO:625),
DCVGDLVASVAWLPTWLRGSATHKCPGL (SEQ ID NO:626),
DDRPRVQHQAHLDSLAVVHLHHMEPEAVDTPDRGYEGARGPVKATALVHQ
DLVEVDGPTGAIAGFPCWLMVVASDRXKCHSPRGCLSQGCSPGPPCSSSARL
TDHQALPLQQDGL (SEQ ID NO:627),
YEGARGPVKATALVHQDLVEVDGPTGAIAGF (SEQ ID NO:628),
MAPLVPLPVSPAGSWWWLRTAXNATRPGGASPRAAPPGPPAAARPGSQTTR
HSPSSRTGSDPSWAHPAPRARSTRTKGSPGLCRGPGSQCGLAPNMAEGLCNP
QVPRSSAPLLFPLLSLDSHRRHPDSLPSLGSLNPLSIPVSQLCPASHSYSCCHCS
S (SEQ ID NO:629), SSRTGSDPSWAHPAPRARSTRTKGSPGLC (SEQ ID
NO:630), and/or RRHPDSLPSLGSLNPLSIPVSQLCPAS (SEQ ID NO:631).
Moreover, fragments and variants of these polypeptides (such as, for example, fragments as described herein, polypeptides at least 80%, 85%, 90%, 95%, 96%, 97%, 98%, or 99% identical to these polypeptides and polypeptides encoded by the polynucleotide which hybridizes, under stringent conditions, to the polynucleotide encoding these polypeptides) are encompassed by the invention. Antibodies that bind polypeptides of the invention are also encompassed by the invention. Polynucleotides encoding these polypeptides are also encompassed by the invention.

This gene is expressed primarily in cerebellum and infant brain. By Northern analysis, a single transcript of 2.4 kb was observed in brain tissues.

Polynucleotides and polypeptides of the invention are useful as reagents for differential identification of the tissue(s) or cell type(s) present in a biological sample and for diagnosis of diseases and conditions which include, but are not limited to, neural and developmental disorders, particularly neuronal cell signal transduction, synaptic physiology, or proliferative conditions such as cancer. Similarly, polypeptides and antibodies directed to these polypeptides are useful in providing immunological probes for differential identification of the tissue(s) or cell type(s).

FEDOCID: WO 0059951A1

For a number of disorders of the above tissues or cells, particularly of the neuronal cell signal transduction and synaptic physiology expression of this gene at significantly higher or lower levels may be routinely detected in certain tissues or cell types (e.g., neural, developmental, and cancerous and wounded tissues) or bodily fluids (e.g., lymph, amniotic fluid, serum, plasma, urine, synovial fluid and spinal fluid) or another tissue or cell sample taken from an individual having such a disorder, relative to the standard gene expression level, i.e., the expression level in healthy tissue or bodily fluid from an individual not having the disorder.

The tissue distribution in cerebellum and infant brain, combined with the homology to the conserved precerebellin gene or gene family indicates that the protein product of this gene is useful for diagnosis and treatment of neuronal cell related disorders. Furthermore, the protein product of this gene is useful for the detection/treatment of neurodegenerative disease states, behavioral disorders, or inflammatory conditions such as Alzheimer's Disease, Parkinson's Disease, Huntington's Disease, Tourette's Syndrome, meningitis, encephalitis, demyelinating diseases, peripheral neuropathies, neoplasia, trauma, congenital malformations, spinal cord injuries, ischemia and infarction, aneurysms, hemorrhages, schizophrenia, mania, dementia, paranoia, obsessive compulsive disorder, panic disorder, learning disabilities, ALS, psychoses, autism, and altered behaviors, including disorders in feeding, sleep patterns, balance, and perception. In addition, elevated expression of this gene product in regions of the brain indicates that it plays a role in normal neural function. Potentially, this gene product is involved in synapse formation, neurotransmission, learning, cognition, homeostasis, or neuronal differentiation or survival. Moreover, the gene or gene product may also play a role in the treatment and/or detection of developmental disorders associated with the developing embryo, sexually-linked disorders, or disorders of the cardiovascular system. Protein, as well as, antibodies directed against the protein may show utility as a tumor marker and/or immunotherapy targets for the above listed tissues.

Many polynucleotide sequences, such as EST sequences, are publicly available and accessible through sequence databases. Some of these sequences are related to SEQ ID NO:55 and may have been publicly available prior to conception of the present invention. Preferably, such related polynucleotides are specifically

excluded from the scope of the present invention. To list every related sequence is cumbersome. Accordingly, preferably excluded from the present invention are one or more polynucleotides comprising a nucleotide sequence described by the general formula of a-b, where a is any integer between 1 to 976 of SEQ ID NO:55, b is an integer of 15 to 990, where both a and b correspond to the positions of nucleotide residues shown in SEQ ID NO:55, and where b is greater than or equal to a + 14.

FEATURES OF PROTEIN ENCODED BY GENE NO: 46

In specific embodiments, polypeptides of the invention comprise, or alternatively consist of, the following amino acid sequences: STHASGPPAPERLCLPERGTAPWGRRANDAA (SEQ ID NO:632), VRRWWLRTMGAAAHCTPEQRRPRRPATILGMDTQNILHTRLSLCSLSWVSL ASSFXXLAXRRKAIVVQQKQSKISKKKKVEKXXLNDSVNENSDTVGQIVHYI MKNEANADVLKAMVADNSLYDPESPVTPSTPGSPPVSPGLCHQGGRQGSTS VAIICIRWAVXSRGMCVIGVGTSGGTL (SEQ ID NO:633), and/or IMKNEANADVLKAMVADNSLYDPESPVTP (SEQ ID NO:634). Moreover, fragments and variants of these polypeptides (such as, for example, fragments as described herein, polypeptides at least 80%, 85%, 90%, 95%, 96%, 97%, 98%, or 99% identical to these polypeptides and polypeptides encoded by the polynucleotide which hybridizes, under stringent conditions, to the polynucleotide encoding these polypeptides) are encompassed by the invention. Antibodies that bind polypeptides of the invention are also encompassed by the invention. Polynucleotides encoding these polypeptides are also encompassed by the invention.

This gene is expressed in fetal liver and spleen, and to a lesser extent in bone marrow, umbilical vein, and T cells.

Polynucleotides and polypeptides of the invention are useful as reagents for differential identification of the tissue(s) or cell type(s) present in a biological sample and for diagnosis of diseases and conditions which include, but are not limited to, disorders of the immune system, particularly hematopoiesis. Similarly, polypeptides and antibodies directed to these polypeptides are useful in providing immunological

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probes for differential identification of the tissue(s) or cell type(s). For a number of disorders of the above tissues or cells, particularly of the hematopoiesis and immune disorders, expression of this gene at significantly higher or lower levels may be routinely detected in certain tissues or cell types (e.g., immune, hematopoietic, developmental, and cancerous and wounded tissues) or bodily fluids (e.g., lymph, amniotic fluid, serum, plasma, urine, synovial fluid and spinal fluid) or another tissue or cell sample taken from an individual having such a disorder, relative to the standard gene expression level, i.e., the expression level in healthy tissue or bodily fluid from an individual not having the disorder.

Predicted epitopes include those comprising a sequence shown in SEQ ID NO: 294 as residues: Asp-30 to Glu-57.

The tissue distribution in fetal liver/spleen and bone marrow indicates that the protein product of this gene is useful for diagnosis and treatment of hematopoietic and immune disorders. Moreover, the protein product of this gene is useful for the treatment and diagnosis of hematopoetic related disorders such as anemia, pancytopenia, leukopenia, thrombocytopenia or leukemia since stromal cells are important in the production of cells of hematopoietic lineages. The uses include bone marrow cell ex vivo culture, bone marrow transplantation, bone marrow reconstitution, radiotherapy or chemotherapy of neoplasia. The gene product may also be involved in lymphopoiesis, therefore, it can be used in immune disorders such as infection, inflammation, allergy, immunodeficiency etc. In addition, this gene product may have commercial utility in the expansion of stem cells and committed progenitors of various blood lineages, and in the differentiation and/or proliferation of various cell types. Protein, as well as, antibodies directed against the protein may show utility as a tumor marker and/or immunotherapy targets for the above listed tissues.

Many polynucleotide sequences, such as EST sequences, are publicly available and accessible through sequence databases. Some of these sequences are related to SEQ ID NO:56 and may have been publicly available prior to conception of the present invention. Preferably, such related polynucleotides are specifically excluded from the scope of the present invention. To list every related sequence is cumbersome. Accordingly, preferably excluded from the present invention are one or

more polynucleotides comprising a nucleotide sequence described by the general formula of a-b, where a is any integer between 1 to 1589 of SEQ ID NO:56, b is an integer of 15 to 1603, where both a and b correspond to the positions of nucleotide residues shown in SEQ ID NO:56, and where b is greater than or equal to a + 14.

FEATURES OF PROTEIN ENCODED BY GENE NO: 47

The translation product of this gene shares sequence homology with a 12 kD nucleic acid binding protein of Feline calcivirus which is thought to be important in viral replication and may implicate this protein as playing an integral role in the development of host-viral inhibitors and/or novel vaccines. (See Genbank Accession No. 59264).

In specific embodiments, polypeptides of the invention comprise, or alternatively consist of, the following amino acid sequences: HCHLWASGSCLACFFPGGLTRDAAQQHVTKSYSPPYLSQTSHSCLVFQPVLW PEYTFWNLFEAILQFQMNHSVLQQXGPRHVCRGAEEAAAGEGPGYSDRAAA ARGAPSQWGRPAPKDTLAQTLGQTGRASPRLPAGLGTQAS (SEQ ID NO:635), PAPKDTLAQTLGQTGRASPRLPAGLGTQ (SEQ ID NO:636), TIACFSXKARDMYAEERKRQQLERDQATVTEQLLREGLQASGDAQLRRTRL HKLSARREERVQGFLQALELKRADWLARLGTASA (SEQ ID NO:637), and/or LRRTRLHKLSARREERVQGFLQALELKR (SEQ ID NO:638). Moreover, fragments and variants of these polypeptides (such as, for example, fragments as described herein, polypeptides at least 80%, 85%, 90%, 95%, 96%, 97%, 98%, or 99% identical to these polypeptides and polypeptides encoded by the polynucleotide which hybridizes, under stringent conditions, to the polynucleotide encoding these polypeptides) are encompassed by the invention. Antibodies that bind polypeptides of the invention are also encompassed by the invention. Polynucleotides encoding these polypeptides are also encompassed by the invention..

This gene is expressed primarily in human cardiomyopathy tissue, and to a lesser extent, in T helper cells, fetal brain and synovial sarcoma.

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Polynucleotides and polypeptides of the invention are useful as reagents for differential identification of the tissue(s) or cell type(s) present in a biological sample and for diagnosis of diseases and conditions which include, but are not limited to, cardiovascular, immune, or developmental disorders, particularly cardiomyopathy which occur secondary to viral infections. Similarly, polypeptides and antibodies directed to these polypeptides are useful in providing immunological probes for differential identification of the tissue(s) or cell type(s). For a number of disorders of the above tissues or cells, particularly of the cardiovascular system, expression of this gene at significantly higher or lower levels may be routinely detected in certain tissues or cell types (e.g., cardiovascular, neural, developmental, skeletal, immune cancerous and wounded tissues) or bodily fluids (e.g., lymph, amniotic fluid, serum, plasma, urine, synovial fluid and spinal fluid) or another tissue or cell sample taken from an individual having such a disorder, relative to the standard gene expression level, i.e., the expression level in healthy tissue or bodily fluid from an individual not having the disorder.

Predicted epitopes include those comprising a sequence shown in SEQ ID NO: 295 as residues: Trp-20 to Cys-26.

The tissue distribution in cardiomyopathy tissue, combined with the homology to a viral 12 kD nucleic acid binding protein indicates that the protein product of this gene is useful for diagnosis and intervention of cardiomyopathy, including those caused by ischemic, hypertensive, congenital, valvular, or pericardial abnormalities. The gene expression pattern may be the consequence or the cause for these conditions. Protein, as well as, antibodies directed against the protein may show utility as a tumor marker and/or immunotherapy targets for the above listed tissues.

Many polynucleotide sequences, such as EST sequences, are publicly available and accessible through sequence databases. Some of these sequences are related to SEQ ID NO:57 and may have been publicly available prior to conception of the present invention. Preferably, such related polynucleotides are specifically excluded from the scope of the present invention. To list every related sequence is cumbersome. Accordingly, preferably excluded from the present invention are one or more polynucleotides comprising a nucleotide sequence described by the general formula of a-b, where a is any integer between 1 to 1038 of SEQ ID NO:57, b is an

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integer of 15 to 1052, where both a and b correspond to the positions of nucleotide residues shown in SEQ ID NO:57, and where b is greater than or equal to a + 14.

FEATURES OF PROTEIN ENCODED BY GENE NO: 48

The translation product of this gene shares sequence homology with tumor necrosis factor related gene product, which is thought to be important in tumor necrosis, bacterial and viral infection, immune diseases and immunoreactions.

In specific embodiments, polypeptides of the invention comprise, or alternatively consist of, the following amino acid sequences: KMNSIPWQIPKITPXLDANLVIVECKPLWFCIGTIKQLKLWNQVFMGFKSMFF RIGKLNYLFTIPYCYLFIDNILGIFYSILGAQGIKYNFYIQRIFTCLLNLNLKIHSN LA (SEQ ID NO:639), LWFCIGTIKQLKLWNQVFMGFKSMFFR (SEQ ID NO:640), YSILGAQGIKYNFYIQRIFTCLLNLN (SEQ ID NO:641), and/or TFKLVRFLE (SEQ ID NO:642). Moreover, fragments and variants of these polypeptides (such as, for example, fragments as described herein, polypeptides at least 80%, 85%, 90%, 95%, 96%, 97%, 98%, or 99% identical to these polypeptides and polypeptides encoded by the polynucleotide which hybridizes, under stringent conditions, to the polynucleotide encoding these polypeptides) are encompassed by the invention. Antibodies that bind polypeptides of the invention are also encompassed by the invention. Polynucleotides encoding these polypeptides are also encompassed by the invention.

The gene encoding the disclosed cDNA is believed to reside on chromosome 10. Accordingly, polynucleotides related to this invention are useful as a marker in linkage analysis for chromosome 10.

This gene is expressed primarily in colon, and to a lesser extent, in ovarian and breast cancers.

Polynucleotides and polypeptides of the invention are useful as reagents for differential identification of the tissue(s) or cell type(s) present in a biological sample and for diagnosis of diseases and conditions which include, but are not limited to, gastrointestinal, reproductive, colon, ovarian, breast disorders, particularly cancers.

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Similarly, polypeptides and antibodies directed to these polypeptides are useful in providing immunological probes for differential identification of the tissue(s) or cell type(s). For a number of disorders of the above tissues or cells, particularly of the colon, ovary and breast, expression of this gene at significantly higher or lower levels may be routinely detected in certain tissues or cell types (e.g., gastrointestinal, reproductive, colon, ovarian, breast, and cancerous and wounded tissues) or bodily fluids (e.g., lymph, breast milk, bile, serum, plasma, urine, synovial fluid and spinal fluid) or another tissue or cell sample taken from an individual having such a disorder, relative to the standard gene expression level, i.e., the expression level in healthy tissue or bodily fluid from an individual not having the disorder.

The tissue distribution in colon tissue, combined with the homology to tumor necrosis factors indicates that the protein product of this gene is useful for the intervention of cancers of the colon, ovary and breast, particularly because TNF family members are known to be involved in the tumor development. Protein, as well as, antibodies directed against the protein may show utility as a tumor marker and/or immunotherapy targets for the above listed tissues.

Many polynucleotide sequences, such as EST sequences, are publicly available and accessible through sequence databases. Some of these sequences are related to SEQ ID NO:58 and may have been publicly available prior to conception of the present invention. Preferably, such related polynucleotides are specifically excluded from the scope of the present invention. To list every related sequence is cumbersome. Accordingly, preferably excluded from the present invention are one or more polynucleotides comprising a nucleotide sequence described by the general formula of a-b, where a is any integer between 1 to 800 of SEQ ID NO:58, b is an integer of 15 to 814, where both a and b correspond to the positions of nucleotide residues shown in SEQ ID NO:58, and where b is greater than or equal to a + 14.

FEATURES OF PROTEIN ENCODED BY GENE NO: 49

The translation product of this gene shares sequence homology with mucins, such as epithelial mucin, which are thought to be important in extracellular matrix

functions such as protection, lubrication and cell adhesion, which are important in a variety of functions, particularly immune chemotaxis and infiltration (See for example Genbank Accession No. R68002).

In specific embodiments, polypeptides of the invention comprise, or alternatively consists of, an amino acid sequence selected from the group: PRSRPALRPGRQRPPSHSATSGVLRPRKKPDP (SEQ ID NO:643), RKSFAKPVLWTNAIQAGRGRVLCYTRPPPASSSFSALVPDGNRMEGLRTYFL NAFDPGTDYLYLFPFSFTVTFQHCLTVRWAFESLQVPQNRPERWASHPLPTH XPAYLPDNQVXMSASG (SEQ ID NO:644), GNRMEGLRTYFLNAFDPGTDYLYLF (SEQ ID NO:645), and/or FQHCLTVRWAFESLQVPQNRPERWASHPLP (SEQ ID NO:646). Moreover, fragments and variants of these polypeptides (such as, for example, fragments as described herein, polypeptides at least 80%, 85%, 90%, 95%, 96%, 97%, 98%, or 99% identical to these polypeptides and polypeptides encoded by the polynucleotide which hybridizes, under stringent conditions, to the polynucleotide encoding these polypeptides) are encompassed by the invention. Antibodies that bind polypeptides of the invention are also encompassed by the invention. Polynucleotides encoding these polypeptides are also encompassed by the invention.

Moreover, this gene maps to chromosome 22q11.2-qter, and therefore, can be used as a marker in linkage analysis for chromosome 22.

This gene is expressed primarily in corpus colosum.

Polynucleotides and polypeptides of the invention are useful as reagents for differential identification of the tissue(s) or cell type(s) present in a biological sample and for diagnosis of diseases and conditions which include, but are not limited to, tumors, especially of the corpus colosum, as well as metastatic lesions, autoimmune conditions, and integumentary disorders. Similarly, polypeptides and antibodies directed to these polypeptides are useful in providing immunological probes for differential identification of the tissue(s) or cell type(s). For a number of disorders of the above tissues or cells, particularly of the corpus colosum and other solid tissues, expression of this gene at significantly higher or lower levels may be routinely detected in certain tissues or cell types (e.g., integumentary, autoimmune, neural, and cancerous and wounded tissues) or bodily fluids (e.g., lymph, serum, plasma, urine,

synovial fluid and spinal fluid) or another tissue or cell sample taken from an individual having such a disorder, relative to the standard gene expression level, i.e., the expression level in healthy tissue or bodily fluid from an individual not having the disorder.

The tissue distribution in corpus colosum, combined with the homology to mucins indicates that the protein product of this gene is useful for serum tumor markers or immunotherapy targets because tumor cells have greatly elevated levels of mucin expression and shed the molecules into the epithelial tissues. Moreover, the protein product of this gene is useful for the treatment, diagnosis, and/or prevention of various skin disorders including congenital disorders (i.e. nevi, moles, freckles, Mongolian spots, hemangiomas, port-wine syndrome), integumentary tumors (i.e. keratoses, Bowen's disease, basal cell carcinoma, squamous cell carcinoma, malignant melanoma, Paget's disease, mycosis fungoides, and Kaposi's sarcoma), injuries and inflammation of the skin (i.e. wounds, rashes, prickly heat disorder, psoriasis, dermatitis), atherosclerosis, uticaria, eczema, photosensitivity, autoimmune disorders (i.e. lupus erythematosus, vitiligo, dermatomyositis, morphea, scleroderma, pemphigoid, and pemphigus), keloids, striae, erythema, petechiae, purpura, and xanthelasma. In addition, such disorders may predispose increased susceptibility to viral and bacterial infections of the skin (i.e. cold sores, warts, chickenpox, molluscum contagiosum, herpes zoster, boils, cellulitis, erysipelas, impetigo, tinea, Althlete's foot, and ringworm). Moreover, the protein product of this gene may also be useful for the treatment or diagnosis of various connective tissue disorders such as arthritis, trauma, tendonitis, chrondomalacia and inflammation, autoimmune disorders such as rheumatoid arthritis, lupus, scleroderma, and dermatomyositis as well as dwarfism, spinal deformation, and specific joint abnormalities as well as chondrodysplasias (i.e. spondyloepiphyseal dysplasia congenita, familial osteoarthritis, Atelosteogenesis type II, metaphyseal chondrodysplasia type Schmid). Protein, as well as, antibodies directed against the protein may show utility as a tumor marker and/or immunotherapy targets for the above listed tissues.

Many polynucleotide sequences, such as EST sequences, are publicly available and accessible through sequence databases. Some of these sequences are related to SEQ ID NO:59 and may have been publicly available prior to conception of

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the present invention. Preferably, such related polynucleotides are specifically excluded from the scope of the present invention. To list every related sequence is cumbersome. Accordingly, preferably excluded from the present invention are one or more polynucleotides comprising a nucleotide sequence described by the general formula of a-b, where a is any integer between 1 to 1201 of SEQ ID NO:59, b is an integer of 15 to 1215, where both a and b correspond to the positions of nucleotide residues shown in SEQ ID NO:59, and where b is greater than or equal to a + 14.

FEATURES OF PROTEIN ENCODED BY GENE NO: 50

This gene is expressed primarily in CD34 depleted buffy coat cord blood and primary dendritic cells.

Polynucleotides and polypeptides of the invention are useful as reagents for differential identification of the tissue(s) or cell type(s) present in a biological sample and for diagnosis of diseases and conditions which include, but are not limited to, hematopoietic disorders and immunological disorders, particularly those related to developmental or reproductive conditions. Similarly, polypeptides and antibodies directed to these polypeptides are useful in providing immunological probes for differential identification of the tissue(s) or cell type(s). For a number of disorders of the above tissues or cells, particularly of the hematopoietic and immune systems, expression of this gene at significantly higher or lower levels may be routinely detected in certain tissues or cell types (e.g., developmental, immune, hematopoietic, and cancerous and wounded tissues) or bodily fluids (e.g., lymph, amniotic fluid, serum, plasma, urine, synovial fluid and spinal fluid) or another tissue or cell sample taken from an individual having such a disorder, relative to the standard gene expression level, i.e., the expression level in healthy tissue or bodily fluid from an individual not having the disorder.

The tissue distribution in CD34 depleted buffy coat cord blood and primary dendritic cells indicates that the protein product of this gene is useful for the diagnosis and treatment of hematopoietic and immune disorders. Secreted or cell surface proteins in the above tissue distribution often are involved in cell activation (e.g.

cytokines) or molecules involved in cell surface activation. Moreover, the protein product of this gene is useful for the treatment and diagnosis of hematopoetic related disorders such as anemia, pancytopenia, leukopenia, thrombocytopenia or leukemia since stromal cells are important in the production of cells of hematopoietic lineages. The uses include bone marrow cell ex vivo culture, bone marrow transplantation, bone marrow reconstitution, radiotherapy or chemotherapy of neoplasia. The gene product may also be involved in lymphopoiesis, therefore, it can be used in immune disorders such as infection, inflammation, allergy, immunodeficiency etc. In addition, this gene product may have commercial utility in the expansion of stem cells and committed progenitors of various blood lineages, and in the differentiation and/or proliferation of various cell types. Protein, as well as, antibodies directed against the protein may show utility as a tumor marker and/or immunotherapy targets for the above listed tissues.

Many polynucleotide sequences, such as EST sequences, are publicly available and accessible through sequence databases. Some of these sequences are related to SEQ ID NO:60 and may have been publicly available prior to conception of the present invention. Preferably, such related polynucleotides are specifically excluded from the scope of the present invention. To list every related sequence is cumbersome. Accordingly, preferably excluded from the present invention are one or more polynucleotides comprising a nucleotide sequence described by the general formula of a-b, where a is any integer between 1 to 464 of SEQ ID NO:60, b is an integer of 15 to 478, where both a and b correspond to the positions of nucleotide residues shown in SEQ ID NO:60, and where b is greater than or equal to a + 14.

FEATURES OF PROTEIN ENCODED BY GENE NO: 51

The translation product of this gene shares sequence homology with Interferon induced 1-8 gene encoded polypeptide, which is thought to be important in binding to retroviral rev responsive elements and may be beneficial in the development of novel inhibitors of host-viral interactions leading to effective viral vaccines.

In specific embodiments, polypeptides of the invention comprise, or alternatively consists of, an amino acid sequence selected from the group: MTLITPSXKLTFXKGNKSWSSRACSSTLVDP (SEQ ID NO:647), FLFLHAVDPWPSNG (SEQ ID NO:648), WSCQSGVFLVFTGCSVLCQMLSGAVVVWRRSAPEDSAVWQASINKPRGKGR HGIKGENTSV (SEQ ID NO:649), and/or LVFTGC SVLCQMLSGAVVVWRRSAPEDSAVWQASI (SEQ ID NO:650). Moreover, fragments and variants of these polypeptides (such as, for example, fragments as described herein, polypeptides at least 80%, 85%, 90%, 95%, 96%, 97%, 98%, or 99% identical to these polypeptides and polypeptides encoded by the polynucleotide which hybridizes, under stringent conditions, to the polynucleotide encoding these polypeptides) are encompassed by the invention. Antibodies that bind polypeptides of the invention are also encompassed by the invention. Polynucleotides encoding these polypeptides are also encompassed by the invention.

This gene is expressed primarily in CD34 positive cells and neutrophils.

Polynucleotides and polypeptides of the invention are useful as reagents for differential identification of the tissue(s) or cell type(s) present in a biological sample and for diagnosis of diseases and conditions which include, but are not limited to, viral infection, such as AIDS, and other immune or hematopoietic disorders. Similarly, polypeptides and antibodies directed to these polypeptides are useful in providing immunological probes for differential identification of the tissue(s) or cell type(s). For a number of disorders of the above tissues or cells, particularly of the immune system, expression of this gene at significantly higher or lower levels may be routinely detected in certain tissues or cell types (e.g., immune, hematopoietic, and cancerous and wounded tissues) or bodily fluids (e.g., lymph, amniotic fluid, serum, plasma, urine, synovial fluid and spinal fluid) or another tissue or cell sample taken from an individual having such a disorder, relative to the standard gene expression level, i.e., the expression level in healthy tissue or bodily fluid from an individual not having the disorder.

Predicted epitopes include those comprising a sequence shown in SEQ ID NO: 299 as residues: Gln-51 to Trp-62.

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The tissue distribution in neutrophils and CD34 positive cells, combined with the homology to interferon induced gene 1-8 indicates that the protein product of this gene is useful for the intervention of retroviral infection including HIV. The factor may be involved in viral stability or viral entry into the cells. Alternatively, the virus/factor complex may elicit the cellular immune reaction and could possibly play a beneficial role in the development of effective inhibitors of host-viral interactions, such as exists for novel viral vaccines. Moreover, this gene product may be involved in the regulation of cytokine production, antigen presentation, or other processes that may also suggest a usefulness in the treatment of cancer (e.g. by boosting immune responses). Since the gene is expressed in cells of lymphoid origin, the natural gene product may be involved in immune functions. Therefore it may be also used as an agent for immunological disorders including arthritis, asthma, immunodeficiency diseases such as AIDS, leukemia, rheumatoid arthritis, granulomatous disease, inflammatory bowel disease, sepsis, acne, neutropenia, neutrophilia, psoriasis, hypersensitivities, such as T-cell mediated cytotoxicity; immune reactions to transplanted organs and tissues, such as host-versus-graft and graft-versus-host diseases, or autoimmunity disorders, such as autoimmune infertility, lens tissue injury, demyelination, systemic lupus erythematosis, drug induced hemolytic anemia, rheumatoid arthritis, Sjogren's disease, scleroderma and tissues. In addition, this gene product may have commercial utility in the expansion of stem cells and committed progenitors of various blood lineages, and in the differentiation and/or proliferation of various cell types. Protein, as well as, antibodies directed against the protein may show utility as a tumor marker and/or immunotherapy targets for the above listed tissues.

Many polynucleotide sequences, such as EST sequences, are publicly available and accessible through sequence databases. Some of these sequences are related to SEQ ID NO:61 and may have been publicly available prior to conception of the present invention. Preferably, such related polynucleotides are specifically excluded from the scope of the present invention. To list every related sequence is cumbersome. Accordingly, preferably excluded from the present invention are one or more polynucleotides comprising a nucleotide sequence described by the general formula of a-b, where a is any integer between 1 to 604 of SEQ ID NO:61, b is an

integer of 15 to 618, where both a and b correspond to the positions of nucleotide residues shown in SEQ ID NO:61, and where b is greater than or equal to a + 14.

FEATURES OF PROTEIN ENCODED BY GENE NO: 52

This gene shares sequence homology to immunoglobulin lambda chain (See Genbank Accession No. 2865484). Therefore it is likely that this gene has activity similar to an immunoglobulin lambda chain and may play a beneficial role in the development of effective immunotherapy-based toxins.

In specific embodiments, polypeptides of the invention comprise, or alternatively consists of, an amino acid sequence selected from the group: GHPSPALSIAPSDGSQLPCDEVPYGEAHVTRYCKKPLTNSHLETEAQSSSL (SEQ ID NO:651), NNKHYLSFCGSGFCPVYLGFTGLASHQAVKVLVVAVIIPRQDRERICLQAQV GRIHLRGCWTGPPFLDGYWSEAFYNTLSRGPLHRAPHHMATGFHQREQWKE QEKGDQGRHRSLLVASPQKRCYFCCILXVRSESLGPGVEFYXGVNGRR (SEQ ID NO:652), ERICLQAQVGRIHLRGCWTGPPFLDGYWSEAF (SEQ ID NO:653), SDGSQLPCDEVPYGEAHVTRYCKKPL (SEQ ID NO:654), and/or HQREQWKEQEKGDQGRHRSLLVASPQK (SEQ ID NO:655). Moreover, fragments and variants of these polypeptides (such as, for example, fragments as described herein, polypeptides at least 80%, 85%, 90%, 95%, 96%, 97%, 98%, or 99% identical to these polypeptides and polypeptides encoded by the polynucleotide which hybridizes, under stringent conditions, to the polynucleotide encoding these polypeptides) are encompassed by the invention. Antibodies that bind polypeptides of the invention are also encompassed by the invention. Polynucleotides encoding these polypeptides are also encompassed by the invention.

This gene is expressed primarily in Hodgkin's lymphoma.

Polynucleotides and polypeptides of the invention are useful as reagents for differential identification of the tissue(s) or cell type(s) present in a biological sample and for diagnosis of diseases and conditions which include, but are not limited to, Hodgkin's lymphoma and other immune or hematopoietic disorders. Similarly,

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polypeptides and antibodies directed to these polypeptides are useful in providing immunological probes for differential identification of the tissue(s) or cell type(s). For a number of disorders of the above tissues or cells, particularly of the immune system, expression of this gene at significantly higher or lower levels may be routinely detected in certain tissues or cell types (e.g., immune, hematopoietic, and cancerous and wounded tissues) or bodily fluids (e.g., lymph, serum, plasma, urine, synovial fluid and spinal fluid) or another tissue or cell sample taken from an individual having such a disorder, relative to the standard gene expression level, i.e., the expression level in healthy tissue or bodily fluid from an individual not having the disorder.

Predicted epitopes include those comprising a sequence shown in SEQ ID NO: 300 as residues: Pro-27 to Thr-32.

The tissue distribution in Hodgkin's lymphoma, combined with the sequence homology to immunoglobulin lambda chain protein indicates that the protein product of this gene is useful for the diagnosis of Hodgkin's lymphoma, since the elevated expression and secretion by the tumor mass may be indicative of tumors of this type. Additionally the gene product may be used as a target in the immunotherapy of the cancer. Because the gene is expressed in cells of lymphoid origin, the natural gene product may be involved in immune functions. Therefore it may be also used as an agent for immunological disorders including arthritis, asthma, immune deficiency diseases such as AIDS, and leukemia. Protein, as well as, antibodies directed against the protein may show utility as a tumor marker and/or immunotherapy targets for the above listed tissues.

Many polynucleotide sequences, such as EST sequences, are publicly available and accessible through sequence databases. Some of these sequences are related to SEQ ID NO:62 and may have been publicly available prior to conception of the present invention. Preferably, such related polynucleotides are specifically excluded from the scope of the present invention. To list every related sequence is cumbersome. Accordingly, preferably excluded from the present invention are one or more polynucleotides comprising a nucleotide sequence described by the general formula of a-b, where a is any integer between 1 to 737 of SEQ ID NO:62, b is an

integer of 15 to 751, where both a and b correspond to the positions of nucleotide residues shown in SEQ ID NO:62, and where b is greater than or equal to a + 14.

FEATURES OF PROTEIN ENCODED BY GENE NO: 53

This gene has extensive homology to cDNA for Homo sapiens mRNA for the ISLR gene(See Genbank Accession No. AB003184). This protein is considered to be a new member of the Ig superfamily and contains a leucine-rich repeat (LRR) with conserved flanking sequences and a C2-type immunoglobulin (Ig)-like domain. These domains are important for protein-protein interaction or cell adhesion, and therefore it is possible that the novel protein ISLR may also interact with other proteins or cells. The ISLR gene was mapped on human chromosome 15q23-q24 by fluorescence in situ hybridization (See Medline Article No. 97468140). Homology to the ISLR gene has been confirmed by another independent group as well (See Genbank Accession No. Hs.102171).

This gene is expressed in a number of tissues including human retina, heart, skeletal muscle, prostate, ovary, small intestine, thyroid, adrenal cortex, testis, stomach, spinal cord, fetal lung and fetal kidney tissues, colon, tonsil and stomach cancer, and to a lesser extent in endometrial stromal cells treated with estradiol, breast tissue, synovium, lymphoma, and number of other tumors.

Polynucleotides and polypeptides of the invention are useful as reagents for differential identification of the tissue(s) or cell type(s) present in a biological sample and for diagnosis of diseases and conditions which include, but are not limited to, tumors of colon, ovary, breast, and integumentary or immune origins. However, due to the wide range of expression in various tissues, protein may play a vital role in the development of cancer in other tissues as well, not just those mentioned above. Similarly, polypeptides and antibodies directed to these polypeptides are useful in providing immunological probes for differential identification of the tissue(s) or cell type(s). For a number of disorders of the above tissues or cells, particularly of the colon, ovary and breast, expression of this gene at significantly higher or lower levels may be routinely detected in certain tissues or cell types (e.g., immune,

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integumentary, reproductive, developmental, and cancerous and wounded tissues) or bodily fluids (e.g., lymph, amniotic fluid, breast milk, seminal fluid, bile, serum, plasma, urine, synovial fluid and spinal fluid) or another tissue or cell sample taken from an individual having such a disorder, relative to the standard gene expression level, i.e., the expression level in healthy tissue or bodily fluid from an individual not having the disorder. Additionally, this gene maps to chromosome 15q23-q24, and therefore, can be used as a marker in linkage analysis for chromosome 15.

The tissue distribution in tumors of colon, ovary, and breast origins indicates that the protein product of this gene is useful for the diagnosis and intervention of these tumors, in addition to other tumors where expression has been indicated. The secreted protein can also be used to determine biological activity, to raise antibodies, as tissue markers, to isolate cognate ligands or receptors, to identify agents that modulate their interactions and as nutritional supplements. It may also have a very wide range of biological activities. Typical of these are cytokine, cell proliferation/differentiation modulating activity or induction of other cytokines; immunostimulating/immunosuppressant activities (e.g. for treating human immunodeficiency virus infection, cancer, autoimmune diseases and allergy); regulation of hematopoiesis (e.g. for treating anemia or as adjunct to chemotherapy); stimulation or growth of bone, cartilage, tendons, ligaments and/or nerves (e.g. for treating wounds); stimulation of follicle stimulating hormone (for control of fertility); chemotactic and chemokinetic activities (e.g. for treating infections, tumors); hemostatic or thrombolytic activity (e.g. for treating hemophilia, cardiac infarction, etc.); anti-inflammatory activity (e.g. for treating septic shock, Crohn's disease); as antimicrobials; for treating psoriasis or other hyperproliferative diseases; for regulation of metabolism, and behavior. Also contemplated is the use of the corresponding nucleic acid in gene therapy procedures. Protein, as well as, antibodies directed against the protein may show utility as a tumor marker and/or immunotherapy targets for the above listed tissues.

Many polynucleotide sequences, such as EST sequences, are publicly available and accessible through sequence databases. Some of these sequences are related to SEQ ID NO:63 and may have been publicly available prior to conception of the present invention. Preferably, such related polynucleotides are specifically

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excluded from the scope of the present invention. To list every related sequence is cumbersome. Accordingly, preferably excluded from the present invention are one or more polynucleotides comprising a nucleotide sequence described by the general formula of a-b, where a is any integer between 1 to 766 of SEQ ID NO:63, b is an integer of 15 to 780, where both a and b correspond to the positions of nucleotide residues shown in SEQ ID NO:63, and where b is greater than or equal to a + 14.

FEATURES OF PROTEIN ENCODED BY GENE NO: 54

The gene has homology to a multidrug resistance gene 1 (See Genbank Accession No. P06795).

Preferred polynucleotide fragments comprise the following sequence: gcttcgtgtccaaccctcttgcccttcgcctgtgtgcctggagccagtcccaccacgctcgcgtttcctcctgtagtgctcaca ggtcccagcaccgatggcattcccttgccctgagtctgcagcgggtccctttgtgcttccttcccctcaggtagcctctctc cccctgggccactcccgggggtgagggggttaccccttcccagtgtttttattcctgtggggctcaccccaaagtattaaaa gtagctttgtaa (SEQ ID NO:656),
gcttcgtgtccaaccctcttgcccttcgcctgtgtgcctggagccagtcccaccacgctcgcgtttcctcctgtagtgctcaca ggtcccagcaccgatggcattcccttgccctgagtctgcagcgggtccctttgtgcttccttcccctcaggtagcctctctc cccctgggccactcccgggggtgagggggttaccccttcccagtgtttttattcctgtggggctcaccccaaagtattaaaa gtagctttgtaa (SEQ ID NO:657),
gcttcgtgtccaaccctcttgcccttcgcctgtgtgcctggagccagtcccaccacgctcgcgtttcctcctgtagtgctcaca ggtcccagcaccgatggcattcccttgccctgagtctgcagcgggtccctttgtgcttccttcccctcaggtagcctctctc cccctgggccactcccgggggtgagggggttaccccttcccagtgtttttattcctgtggggctcaccccaaagtattaaaa gtagctttgtaa (SEQ ID NO:658). Also preferred are polypeptides comprising one or more of the fragments encoded by these polynucleotide fragments.

In specific embodiments, polypeptides of the invention comprise, or alternatively consists of, an amino acid sequence selected from the group: FRINRLTIGXAVAMTRGNQRELARQKNMKKQSDSVKGKRRDDGLSAAARK QRDSEI (SEQ ID NO:659), AVAMTRGNQRELARQKNMKKQSDSVKGKR (SEQ ID NO:660),
KSRATRLRESAEMTGFLLPPASRGTRRSCSRSRKRQTRRRRNPSSFVASCPTLL

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PFACVPGASPTTLAFPPVVLTGPSTDGIPFALSLQRVPFVLPSPQVASLPLGHSR G (SEQ ID NO:661), LRESAEMTGFLLPPASRGTRRSCSRS (SEQ ID NO:662), and/or VVLTGPSTDGIPFALSLQRVPFVLPSPQVA (SEQ ID NO:663). Moreover, fragments and variants of these polypeptides (such as, for example, fragments as described herein, polypeptides at least 80%, 85%, 90%, 95%, 96%, 97%, 98%, or 99% identical to these polypeptides and polypeptides encoded by the polynucleotide which hybridizes, under stringent conditions, to the polynucleotide encoding these polypeptides) are encompassed by the invention. Antibodies that bind polypeptides of the invention are also encompassed by the invention. Polynucleotides encoding these polypeptides are also encompassed by the invention.

This gene is expressed primarily in lung, esophagus, leukemia (Jurkat cells), breast cancers and to a lesser extent, in macrophages treated with GM-CSF fetal tissues.

Polynucleotides and polypeptides of the invention are useful as reagents for differential identification of the tissue(s) or cell type(s) present in a biological sample and for diagnosis of diseases and conditions which include, but are not limited to, immune, developmental, or pulmonary disorders, particularly cancers. Similarly, polypeptides and antibodies directed to these polypeptides are useful in providing immunological probes for differential identification of the tissue(s) or cell type(s). For a number of disorders of the above tissues or cells, particularly of the solid tumors, lung and leukemia, expression of this gene at significantly higher or lower levels may be routinely detected in certain tissues or cell types (e.g., immune, developmental, pulmonary, and cancerous and wounded tissues) or bodily fluids (e.g., lymph, pulmonary surfactant and sputum, amniotic fluid, serum, plasma, urine, synovial fluid and spinal fluid) or another tissue or cell sample taken from an individual having such a disorder, relative to the standard gene expression level, i.e., the expression level in healthy tissue or bodily fluid from an individual not having the disorder. Furthermore, due to the high expression level in lung tissue and the proposed function of the multidrug resistance protein 1 gene as the efflux pump responsible for low-drug accumulation in multidrug-resistant cells, protein as well mutants thereof, may also be beneficial as a target for gene therapy, particularly for the chronic patient.

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Predicted epitopes include those comprising a sequence shown in SEQ ID NO: 302 as residues: Met-1 to Lys-16.

The tissue distribution cancers and fetal tissues indicates that the protein product of this gene is useful for the detection of cells in active proliferation, such as cancers. The gene products may be used for cancer markers or immunotherapy target. Similarly, the secreted protein can also be used to determine biological activity, to raise antibodies, as tissue markers, to isolate cognate ligands or receptors, to identify agents that modulate their interactions and as nutritional supplements. It may also have a very wide range of biological activities. Typical of these are cytokine, cell proliferation/differentiation modulating activity or induction of other cytokines; immunostimulating/immunosuppressant activities (e.g. for treating human immunodeficiency virus infection, cancer, autoimmune diseases and allergy); regulation of hematopoiesis (e.g. for treating anemia or as adjunct to chemotherapy); stimulation or growth of bone, cartilage, tendons, ligaments and/or nerves (e.g. for treating wounds); stimulation of follicle stimulating hormone (for control of fertility); chemotactic and chemokinetic activities (e.g. for treating infections, tumors); hemostatic or thrombolytic activity (e.g. for treating hemophilia, cardiac infarction, etc.); anti-inflammatory activity (e.g. for treating septic shock, Crohn's disease); as antimicrobials; for treating psoriasis or other hyperproliferative diseases; for regulation of metabolism, and behavior. Also contemplated is the use of the corresponding nucleic acid in gene therapy procedures. Protein, as well as, antibodies directed against the protein may show utility as a tumor marker and/or immunotherapy targets for the above listed tissues.

Many polynucleotide sequences, such as EST sequences, are publicly available and accessible through sequence databases. Some of these sequences are related to SEQ ID NO:64 and may have been publicly available prior to conception of the present invention. Preferably, such related polynucleotides are specifically excluded from the scope of the present invention. To list every related sequence is cumbersome. Accordingly, preferably excluded from the present invention are one or more polynucleotides comprising a nucleotide sequence described by the general formula of a-b, where a is any integer between 1 to 574 of SEQ ID NO:64, b is an

integer of 15 to 588, where both a and b correspond to the positions of nucleotide residues shown in SEQ ID NO:64, and where b is greater than or equal to a + 14.

FEATURES OF PROTEIN ENCODED BY GENE NO: 55

In specific embodiments, polypeptides of the invention comprise, or alternatively consists of, an amino acid sequence selected from the group: LLSTSHLLTQSYSFNKRSHSFAWKNAHCILQSENNELQNSVYIYVCIYVHF ICTFLCDI (SEQ ID NO:664), and/or KRSHSFAWKNAHCILQSENNELQNSVYIY VCI (SEQ ID NO:665). Moreover, fragments and variants of these polypeptides (such as, for example, fragments as described herein, polypeptides at least 80%, 85%, 90%, 95%, 96%, 97%, 98%, or 99% identical to these polypeptides and polypeptides encoded by the polynucleotide which hybridizes, under stringent conditions, to the polynucleotide encoding these polypeptides) are encompassed by the invention. Antibodies that bind polypeptides of the invention are also encompassed by the invention. Polynucleotides encoding these polypeptides are also encompassed by the invention.

The gene encoding the disclosed cDNA is believed to reside on the X chromosome. Accordingly, polynucleotides related to this invention are useful as a marker in linkage analysis for the X chromosome.

This gene is expressed primarily in the brain, and to a lesser extent, in the developing embryo.

Polynucleotides and polypeptides of the invention are useful as reagents for differential identification of the tissue(s) or cell type(s) present in a biological sample and for diagnosis of diseases and conditions which include, but are not limited to, neurodegenerative disease states and developmental disorders. Similarly, polypeptides and antibodies directed to these polypeptides are useful in providing immunological probes for differential identification of the tissue(s) or cell type(s). For a number of disorders, including X-linked disorders, of the above tissues or cells, particularly of the neurological, developmental systems, and cardiovascular system, expression of this gene at significantly higher or lower levels may be routinely

detected in certain tissues or cell types (e.g., neural, developmental, and cancerous and wounded tissues) or bodily fluids (e.g., lymph, amniotic fluid, serum, plasma, urine, synovial fluid and spinal fluid) or another tissue or cell sample taken from an individual having such a disorder, relative to the standard gene expression level, i.e., the expression level in healthy tissue or bodily fluid from an individual not having the disorder.

The tissue distribution in neural tissue indicates that the protein product of this gene is useful for the detection/treatment of neurodegenerative disease states and behavioral disorders such as Alzheimer's Disease, Parkinson's Disease, Huntington's Disease, Klinefelter's, schizophrenia, mania, dementia, paranoia, obsessive compulsive disorder and panic disorder. In addition, the gene or gene product may also play a role in the treatment and/or detection of developmental disorders associated with the developing embryo, sexually- or X-linked disorders, or disorders of the cardiovascular system. Protein, as well as, antibodies directed against the protein may show utility as a tumor marker and/or immunotherapy targets for the above listed tissues.

Many polynucleotide sequences, such as EST sequences, are publicly available and accessible through sequence databases. Some of these sequences are related to SEQ ID NO:65 and may have been publicly available prior to conception of the present invention. Preferably, such related polynucleotides are specifically excluded from the scope of the present invention. To list every related sequence is cumbersome. Accordingly, preferably excluded from the present invention are one or more polynucleotides comprising a nucleotide sequence described by the general formula of a-b, where a is any integer between 1 to 931 of SEQ ID NO:65, b is an integer of 15 to 945, where both a and b correspond to the positions of nucleotide residues shown in SEQ ID NO:65, and where b is greater than or equal to a + 14.

FEATURES OF PROTEIN ENCODED BY GENE NO: 56

The translation product of this gene shares sequence homology with paxillin, which is thought to be important in mediating signal transduction from growth factor

receptors to the cytoskeleton. Moreover, in normal hematopoietic cells and myeloid cell lines, tyrosine phosphorylation of paxillin has been shown to be rapidly and transiently induced by interleukin-3 and several other hematopoietic growth factors. The predicted structure of paxillin implicates this molecule in protein-protein interactions involved in signal transduction from growth factor receptors and the BCR/ABL oncogene fusion protein to the cytoskeleton.

Preferred polynucleotide fragments comprise the following sequence: tggctcactgtcttacaatcactgctgtggaatcatgataccacttttagctctttgcatcttccttcagtgtatttttgtttttcaaga ggaagtagattttaactggacaactttgagtactgacatcattgataaataaactggcttgtggtttcaa (SEQ ID NO:666). Also preferred are polypeptide fragments encoded by these polynucleotide fragments.

In specific embodiments, polypeptides of the invention comprise, or alternatively consists of, an amino acid sequence selected from the group: LDELMAHLTEMQAKVAVRADAGKKHLPDKQDHKASLDSMLGGLEQELQDL GIATVPKGHCASCQKPIAGKVIHALGQSWHPEHFVCTHCKEEIGSSPFFERSGL XYCPNDYHQLFSPRCAYCAAPILDKVLTAMNQTWHPEHFFCSHCGEVFGAE GFHEKDKKPYCRKDFLAMFSPKCGGCNRPVLENYLSAMDTVWHPECFVCG DCFTSFSTGSFFELDGRPFCELHYHHRRGTLCHGCGQPITGRCISAMGYKFHP EHFVCAFCLTQLSKGIFREQNDKTYCQPCFNKLF (SEQ ID NO:667), KASLDSMLGGLEQELQDLGIATVPKGHCASCQKPIAGKVIHAL (SEQ ID NO:668), CPNDYHQLFSPRCAYCAAPILDKVLTAMNQTWHPEHFFCSHCGEVFGAEG (SEQ ID NO:669), DKKPYCRKDFLAMFSPKCGGCNRPVLENYLSAMDTVWHPECFVCGDCFTSF STGSFFELDGRPFCEL (SEQ ID NO:670), CGQPITGRCISAMGYKFHPEHFVCAFCLTQLSKGIFREQNDKTYCQ (SEQ ID NO:671), HKSLAGAXVYTTNIQELNVYSEAQEPKESPPPSKTSAAAQLDELMAHLTEMQ AKVAVRADAGKKHLPDKQDHKASLDSMLGGLEQELQDLGIATVPKGHCAS CQKPIAGKVIHALGQSWHPEHFVCTHCKEEIGSSPFFERSGLXYCPNDYHQLF SPRCAYCAAPILDKVLTAMNQTWHPEHFFCSHCGEVFGAEGFHEKDKKPYC RKDFLAMFSPKCGGCNRPVLENYLSAMDTVWHPECFVCGDCFTSFSTGSFFE

LDGRPFCELHYHHRRGTLCHGCGQPITGRCISAMGYKFHPEHFVCAFCLTQLS KGIFREQNDKTYCQPCFNKLFPL (SEQ ID NO:672), NVYSEAQEPKESPPPSKTSAAA (SEQ ID NO:673), DSMLGGLEQELQDLGIATVPKGHCAS (SEQ ID NO:674), YLSAMDTVWHPECFVCGDCFTSFSTG (SEQ ID NO:675), RCISAMGYKFHPEHFVCAFCLTQLSK (SEQ ID NO:676), PTRPVLFFSTCQSCSSRPVRQEHLGCRTMEELDALLEELERSTLQDSDEYSNP APLPLDQHSRKETNLDETSEILSIQDNTSPLPAXSCILPISRSSMSTVKPKSQRN HHHLLKRQQLLSWMSSWLT (SEQ ID NO:677), PVRQEHLGCRTMEELDALLEELERSTLQ (SEQ ID NO:678), SCILPISRSSMSTVKPKSQRN (SEQ ID NO:679), WHPEHFVCTHC (SEQ ID NO:680), LFSPRC (SEQ ID NO:681), PILDKV (SEQ ID NO:682), TWHPEHFF (SEQ ID NO:683), EGFHEKD (SEQ ID NO:684), KFHPEHFVCAFCL (SEQ ID NO:685), PITGRCI (SEQ ID NO:686), and/or HPEHFVC (SEQ ID NO:687). Moreover, fragments and variants of these polypeptides (such as, for example, fragments as described herein, polypeptides at least 80%, 85%, 90%, 95%, 96%, 97%, 98%, or 99% identical to these polypeptides and polypeptides encoded by the polynucleotide which hybridizes, under stringent conditions, to the polynucleotide encoding these polypeptides) are encompassed by the invention. Antibodies that bind polypeptides of the invention are also encompassed by the invention. Polynucleotides encoding these polypeptides are also encompassed by the invention.

The gene encoding the disclosed cDNA is believed to reside on chromosome 11. Accordingly, polynucleotides related to this invention are useful as a marker in linkage analysis for chromosome 11.

This gene is expressed primarily in brain, and to a lesser extent in the developing embryo.

Polynucleotides and polypeptides of the invention are useful as reagents for differential identification of the tissue(s) or cell type(s) present in a biological sample and for diagnosis of diseases and conditions which include, but are not limited to, neurological disease states and developmental abnormalities. Similarly, polypeptides and antibodies directed to these polypeptides are useful in providing immunological probes for differential identification of the tissue(s) or cell type(s). For a number of

disorders of the above tissues or cells, particularly of the immune and nervous systems, expression of this gene at significantly higher or lower levels may be routinely detected in certain tissues or cell types (e.g., neural, developmental, immune, hematopoietic, and cancerous and wounded tissues) or bodily fluids (e.g., lymph, amniotic fluid, serum, plasma, urine, synovial fluid and spinal fluid) or another tissue or cell sample taken from an individual having such a disorder, relative to the standard gene expression level, i.e., the expression level in healthy tissue or bodily fluid from an individual not having the disorder.

The tissue distribution in brain, combined with the homology to the conserved paxillin gene, indicates that the protein product of this gene is useful for the treatment and or detection of disease states associated with abnormal signal transduction in brain and/or the developing embryo. This would include treatment or detection of neurodegenerative disease states and behavioral disorders such as Alzheimer's Disease, Parkinson's Disease, Huntington's Disease, schizophrenia, mania, dementia, paranoia, obsessive compulsive disorder and panic disorder and also in the treatment and or detection of embryonic development defects. Moreover, expression within embryonic tissue and other cellular sources marked by proliferating cells indicates that this protein may play a role in the regulation of cellular division, and may show utility in the diagnosis and treatment of cancer and other proliferative disorders. Similarly, developmental tissues rely on decisions involving cell differentiation and/or apoptosis in pattern formation. Thus this protein may also be involved in apoptosis or tissue differentiation and could again be useful in cancer therapy. Protein, as well as, antibodies directed against the protein may show utility as a tumor marker and/or immunotherapy targets for the above listed tissues.

Many polynucleotide sequences, such as EST sequences, are publicly available and accessible through sequence databases. Some of these sequences are related to SEQ ID NO:66 and may have been publicly available prior to conception of the present invention. Preferably, such related polynucleotides are specifically excluded from the scope of the present invention. To list every related sequence is cumbersome. Accordingly, preferably excluded from the present invention are one or more polynucleotides comprising a nucleotide sequence described by the general formula of a-b, where a is any integer between 1 to 1852 of SEQ ID NO:66, b is an

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integer of 15 to 1866, where both a and b correspond to the positions of nucleotide residues shown in SEQ ID NO:66, and where b is greater than or equal to a + 14.

FEATURES OF PROTEIN ENCODED BY GENE NO: 57

In specific embodiments, polypeptides of the invention comprise, or alternatively consists of, the following amino acid sequence: RIYCSEDTFSPXAESGVSWQSSVSQLYQDYE (SEQ ID NO:688). Moreover, fragments and variants of this polypeptide (such as, for example, fragments as described herein, polypeptides at least 80%, 85%, 90%, 95%, 96%, 97%, 98%, or 99% identical to these polypeptides and polypeptides encoded by the polynucleotide which hybridize, under stringent conditions, to the polynucleotide encoding this polypeptide are encompassed by the invention. Antibodies that bind polypeptides of the invention are also encompassed by the invention. Polynucleotides encoding this polypeptide are also encompassed by the invention.

This gene is expressed primarily in fetal spleen, brain, and to a lesser extent, in six week old embryo.

Polynucleotides and polypeptides of the invention are useful as reagents for differential identification of the tissue(s) or cell type(s) present in a biological sample and for diagnosis of diseases and conditions which include, but are not limited to, immune disorders, neurological disorders, and developmental abnormalities. Similarly, polypeptides and antibodies directed to these polypeptides are useful in providing immunological probes for differential identification of the tissue(s) or cell type(s). For a number of disorders of the above tissues or cells, particularly of the immune and developmental systems, expression of this gene at significantly higher or lower levels may be routinely detected in certain tissues or cell types (e.g., immune, neural, developmental, and cancerous and wounded tissues) or bodily fluids (e.g., lymph, amniotic fluid, serum, plasma, urine, synovial fluid and spinal fluid) or another tissue or cell sample taken from an individual having such a disorder, relative to the standard gene expression level, i.e., the expression level in healthy tissue or bodily fluid from an individual not having the disorder.

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Predicted epitopes include those comprising a sequence shown in SEQ ID NO: 305 as residues: Arg-28 to Gly-34.

The tissue distribution in fetal spleen indicates that the protein product of this gene is useful for the treatment/detection of immune disorders such as arthritis, asthma, immune deficiency diseases such as AIDS, and leukemia. In addition the expression of this gene in the early embryo, indicates a key role in embryo development, and hence the gene or gene product could be used in the treatment and or detection of embryonic developmental defects. This would include treatment or detection of neurodegenerative disease states and behavioral disorders such as Alzheimer's Disease, Parkinson's Disease, Huntington's Disease, schizophrenia, mania, dementia, paranoia, obsessive compulsive disorder and panic disorder and also in the treatment and or detection of embryonic development defects. Protein, as well as, antibodies directed against the protein may show utility as a tumor marker and/or immunotherapy targets for the above listed tissues.

Many polynucleotide sequences, such as EST sequences, are publicly available and accessible through sequence databases. Some of these sequences are related to SEQ ID NO:67 and may have been publicly available prior to conception of the present invention. Preferably, such related polynucleotides are specifically excluded from the scope of the present invention. To list every related sequence is cumbersome. Accordingly, preferably excluded from the present invention are one or more polynucleotides comprising a nucleotide sequence described by the general formula of a-b, where a is any integer between 1 to 1138 of SEQ ID NO:67, b is an integer of 15 to 1152, where both a and b correspond to the positions of nucleotide residues shown in SEQ ID NO:67, and where b is greater than or equal to a + 14.

FEATURES OF PROTEIN ENCODED BY GENE NO: 58

The translation product of this gene shares sequence homology with the gene disrupted in the neurodegenerative disease dentatorubal-pallidoluysian atrophy. Moreover, the translation product of this gene also shares homology with the

GRASP65 protein, a protein involved in the stacking of Golgi cisternae (See Genbank Accession No. AF015264).

In specific embodiments, polypeptides of the invention comprise, or alternatively consists of, an amino acid sequence selected from the group:

MGSSQSVEIPGGGTEGYHVLRVQENSPGHRAGLEPFFDFIVSINGSRLNKDND TLKDLLKXNVEKPVKMLIYSSKTLELRETSVTPSNLWGGQGLLGVSIRFCSFD GANENVWHVLEVESNSPAALAGLRPHSDYIIGADTVMNESEDLFSLIETHEAK PLKLYVYNTDTDNCREVIITPNSAWGGEGSLGCGIGYGYLHRIPTRPFEEGKKI SLPGQMAGTPITPLKDGFTEVQLSSVNPPSLSPPGTTGIEQSLTGLSISSTPPAVS SVLSTGVPTVPLLPPQVNQSLTSVPPMNPATTLPGLMPLPAGLPNLPNLNLNL PAPHIMPGVGLPELVNPGLPPLPSMPPRNLPGIAPLPLPSEFLPSFPLVPESSSAA SSGELLSSLPPTSNAPSDPATTTAKADAASSLTVDVTPPTAKAPTTVEDRVGD STPVSEKPVSAAVDANASESP (SEQ ID NO:689),

SVEIPGGGTEGYHVLRVQENSPGHRAGLEPFFDFIVSINGSRLNKDNDTLKDL LKXNVEKPVKMLIYSSKTLELRETSVTPSNLWGGQGLLGVSIRFCSFDGANEN VWH (SEQ ID NO:690),

ESNSPAALAGLRPHSDYIIGADTVMNESEDLFSLIETHEAKPLKLYVYNTDTD NCREVIITPNSAWGGEGSLGCGIGYGYLHRIPTRPFEEGKKISLPGQMAGTPIT PLKDGFTEVQLSSVNPPSLSPPGTTGIEQSLTGLSISS (SEQ ID NO:691),

ESNSPAALAGLRPHSDYIIGADTVMNESEDLFSLIETHEAKPLKLYVYNTDTD NCREVIITPNSAWGGEGSLGCGIGYGYLHRIPTRPFEEGKKISLPGQMAGTPIT PLKDGFTEVQLSSVNPPSLSPPGTTGIEQSLTGLSISS (SEQ ID NO:692)

RIPTRPFEEGKKISLPGQMAGTPITPLKDGFTEVQLSSVNPPSLSPPGTTGIEQSL TGLSISSTPPAVSSVLSTGVPTVPLLPPQVNQSLTSVPPMNPATTLPGLMPLPA GLPNLPNLNLNLPAPHIMPGVGLPELVNPGLPPLPSMPPRN (SEQ ID NO:693),

PGLPPLPSMPPRNLPGIAPLPLPSEFLPSFPLVPESSSAASSGELLSSLPPTSNAPS DPATTTAKADAASSLTVDVTPPTAKAPTTVEDRVGDSTPVSEKPVSAAVDAN (SEQ ID NO:694), AWGGEGSLGCGIGYGYLHRIPT (SEQ ID NO:695), SPAALAGLRP (SEQ ID NO:696), and/or WGGQGLLG (SEQ ID NO:697).

Moreover, fragments and variants of these polypeptides (such as, for example, fragments as described herein, polypeptides at least 80%, 85%, 90%, 95%, 96%, 97%, 98%, or 99% identical to these polypeptides and polypeptides encoded by the

polynucleotide which hybridizes, under stringent conditions, to the polynucleotide encoding these polypeptides) are encompassed by the invention. Antibodies that bind polypeptides of the invention are also encompassed by the invention. Polynucleotides encoding these polypeptides are also encompassed by the invention.

The gene encoding the disclosed cDNA is believed to reside on chromosome 2. Accordingly, polynucleotides related to this invention are useful as a marker in linkage analysis for chromosome 2.

This gene is expressed primarily in prostate cancer, and to a lesser extent, in the pineal glands and in fetal lung.

Polynucleotides and polypeptides of the invention are useful as reagents for differential identification of the tissue(s) or cell type(s) present in a biological sample and for diagnosis of diseases and conditions which include, but are not limited to, neurological, endocrine, reproductive, pulmonary, developmental disorders. Similarly, polypeptides and antibodies directed to these polypeptides are useful in providing immunological probes for differential identification of the tissue(s) or cell type(s). For a number of disorders of the above tissues or cells, particularly of the nervous, pulmonary, and endocrine systems, expression of this gene at significantly higher or lower levels may be routinely detected in certain tissues or cell types (e.g., neurological, endocrine, reproductive, pulmonary, developmental, and cancerous and wounded tissues) or bodily fluids (e.g., lymph, amniotic fluid, pulmonary surfactant and sputum, serum, plasma, urine, synovial fluid and spinal fluid) or another tissue or cell sample taken from an individual having such a disorder, relative to the standard gene expression level, i.e., the expression level in healthy tissue or bodily fluid from an individual not having the disorder.

Predicted epitopes include those comprising a sequence shown in SEQ ID NO: 306 as residues: Asn-9 to Leu-14.

The abundance of this gene in the pineal gland and its homology to a gene disrupted in the neurodegenerative disease state Dentatorubral-pallidoluysian atrophy indicates that this gene may be useful in the treatment and/or detection of other neurodegenerative disease states and behavioral disorders such as Alzheimer's Disease, Parkinson's Disease, Huntington's Disease, schizophrenia, mania, dementia, paranoia, obsessive compulsive disorder and panic disorder. Alternatively, the

abundance of this gene in fetal lung would suggest that misregulation of the expression of this protein product in the adult could lead to lymphoma or sarcoma formation, particularly in the lung; that it may also be involved in predisposition to certain pulmonary defects such as pulmonary edema and embolism, bronchitis and cystic fibrosis; and thus the gene or the gene product encoded by the gene could be used in the detection and/or treatment of these pulmonary disorders. Protein, as well as, antibodies directed against the protein may show utility as a tumor marker and/or immunotherapy targets for the above listed tissues.

Many polynucleotide sequences, such as EST sequences, are publicly available and accessible through sequence databases. Some of these sequences are related to SEQ ID NO:68 and may have been publicly available prior to conception of the present invention. Preferably, such related polynucleotides are specifically excluded from the scope of the present invention. To list every related sequence is cumbersome. Accordingly, preferably excluded from the present invention are one or more polynucleotides comprising a nucleotide sequence described by the general formula of a-b, where a is any integer between 1 to 2469 of SEQ ID NO:68, b is an integer of 15 to 2483, where both a and b correspond to the positions of nucleotide residues shown in SEQ ID NO:68, and where b is greater than or equal to a + 14.

HOGEN95.0003.0004

FEATURES OF PROTEIN ENCODED BY GENE NO: 59

In specific embodiments, polypeptides of the invention comprise, or alternatively consists of, the following amino acid sequence: RNGALLDKNFFNANSHFPVKGERIRRR (SEQ ID NO:698). Moreover, fragments and variants of this polypeptide (such as, for example, fragments as described herein, polypeptides at least 80%, 85%, 90%, 95%, 96%, 97%, 98%, or 99% identical to these polypeptides and polypeptides encoded by the polynucleotide which hybridize, under stringent conditions, to the polynucleotide encoding this polypeptide are encompassed by the invention. Antibodies that bind polypeptides of the invention are also encompassed by the invention. Polynucleotides encoding this polypeptide are also encompassed by the invention.

This gene is expressed primarily in the developing embryo.

Polynucleotides and polypeptides of the invention are useful as reagents for differential identification of the tissue(s) or cell type(s) present in a biological sample and for diagnosis of diseases and conditions which include, but are not limited to, developmental abnormalities. Similarly, polypeptides and antibodies directed to these polypeptides are useful in providing immunological probes for differential identification of the tissue(s) or cell type(s). For a number of disorders of the above tissues or cells, particularly of the developmental system, expression of this gene at significantly higher or lower levels may be routinely detected in certain tissues or cell types (e.g., developing, proliferating, and cancerous and wounded tissues) or bodily fluids (e.g., lymph, amniotic fluid, serum, plasma, urine, synovial fluid and spinal fluid) or another tissue or cell sample taken from an individual having such a disorder, relative to the standard gene expression level, i.e., the expression level in healthy tissue or bodily fluid from an individual not having the disorder.

The tissue distribution of this gene primarily in the embryo indicates the gene plays a key role in embryo development, and that the gene or the protein encoded by the gene could be used in the treatment and or detection of developmental defects in the embryo or in infants. Similarly, the relatively specific expression of this gene product during embryogenesis indicates that it may be a key player in the proliferation, maintenance, and/or differentiation of various cell types during development. It may also act as a morphogen to control cell and tissue type specification. Because of potential roles in proliferation and differentiation, this gene product may have applications in the adult for tissue regeneration and the treatment of cancers. Expression within embryonic tissue and other cellular sources marked by proliferating cells indicates that this protein may play a role in the regulation of cellular division, and may show utility in the diagnosis and treatment of cancer and other proliferative disorders. Similarly, developmental tissues rely on decisions involving cell differentiation and/or apoptosis in pattern formation. Thus, this protein may also be involved in apoptosis or tissue differentiation and could again be useful in cancer therapy. Protein, as well as, antibodies directed against the protein may show utility as a tumor marker and/or immunotherapy targets for the above listed tissues.

Many polynucleotide sequences, such as EST sequences, are publicly available and accessible through sequence databases. Some of these sequences are related to SEQ ID NO:69 and may have been publicly available prior to conception of the present invention. Preferably, such related polynucleotides are specifically excluded from the scope of the present invention. To list every related sequence is cumbersome. Accordingly, preferably excluded from the present invention are one or more polynucleotides comprising a nucleotide sequence described by the general formula of a-b, where a is any integer between 1 to 522 of SEQ ID NO:69, b is an integer of 15 to 536, where both a and b correspond to the positions of nucleotide residues shown in SEQ ID NO:69, and where b is greater than or equal to a + 14.

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FEATURES OF PROTEIN ENCODED BY GENE NO: 60

This gene displays homology to nestin, an intermediate filament protein, the expression of which correlates with the proliferation of central nervous system progenitor cells and is useful in the identification of brain tumors.

In specific embodiments, polypeptides of the invention comprise, or alternatively consists of, an amino acid sequence selected from the group: RGSGFGWTSFPRPLPTELTCPGFHRERAFPPDGRVRGVRGWGIRRGCRAVWG VGACGCSPGSSWRGSAHRASGPADLPVACRXEGGADSPSLLPSPP (SEQ ID NO:699), AVWGVGACGCSPGSSWRGSAHRA (SEQ ID NO:700), YRP TMEKMKQVVTQTRWMRPDAKRANRRHRRISGKIFAWNPLPKTRFSRLLKAV SENTKRPEPSRPPWMVSHSVEAS (SEQ ID NO:701), and/or FAWNPLPKTRFSRLLKAVSENTKRPEP (SEQ ID NO:702). Moreover, fragments and variants of these polypeptides (such as, for example, fragments as described herein, polypeptides at least 80%, 85%, 90%, 95%, 96%, 97%, 98%, or 99% identical to these polypeptides and polypeptides encoded by the polynucleotide which hybridizes, under stringent conditions, to the polynucleotide encoding these polypeptides) are encompassed by the invention. Antibodies that bind polypeptides of the invention are also encompassed by the invention. Polynucleotides encoding these polypeptides are also encompassed by the invention.

The gene encoding the disclosed cDNA is believed to reside on chromosome 1. Accordingly, polynucleotides related to this invention are useful as a marker in linkage analysis for chromosome 1.

This gene is expressed primarily in kidney, and to a lesser extent, in brain.

Polynucleotides and polypeptides of the invention are useful as reagents for differential identification of the tissue(s) or cell type(s) present in a biological sample and for diagnosis of diseases and conditions which include, but are not limited to, renal disorders and neurodegenerative conditions. Similarly, polypeptides and antibodies directed to these polypeptides are useful in providing immunological probes for differential identification of the tissue(s) or cell type(s). For a number of disorders of the above tissues or cells, particularly of the excretory and nervous systems, expression of this gene at significantly higher or lower levels may be routinely detected in certain tissues or cell types (e.g., neural, urogenital, renal, and cancerous and wounded tissues) or bodily fluids (e.g., lymph, serum, plasma, urine, synovial fluid and spinal fluid) or another tissue or cell sample taken from an individual having such a disorder, relative to the standard gene expression level, i.e., the expression level in healthy tissue or bodily fluid from an individual not having the disorder.

Predicted epitopes include those comprising a sequence shown in SEQ ID NO: 308 as residues: Thr-130 to Asn-137.

The tissue distribution in brain and kidney, combined with the homology to the conserved nestin protein, indicates that the protein product of this gene is useful for the detection and/or treatment of neurodegenerative disease states and behavioral disorders such as Alzheimer's Disease, Parkinson's Disease, Huntington's Disease, schizophrenia, mania, dementia, paranoia, obsessive compulsive disorder and panic disorder. In addition, its abundance in kidney indicates that it is useful in the treatment and detection of acute renal failure and other disease states associated with the kidney, such as nephritus, renal tubular acidosis, proteinuria, pyuria, edema, pyelonephritis, hydronephritis, nephrotic syndrome, crush syndrome, glomerulonephritis, hematuria, renal colic and kidney stones, in addition to Wilms Tumor Disease, and congenital kidney abnormalities such as horseshoe kidney, polycystic kidney, and Falconi's syndrome. Protein, as well as, antibodies directed

against the protein may show utility as a tumor marker and/or immunotherapy targets for the above listed tissues. .

Many polynucleotide sequences, such as EST sequences, are publicly available and accessible through sequence databases. Some of these sequences are related to SEQ ID NO:70 and may have been publicly available prior to conception of the present invention. Preferably, such related polynucleotides are specifically excluded from the scope of the present invention. To list every related sequence is cumbersome. Accordingly, preferably excluded from the present invention are one or more polynucleotides comprising a nucleotide sequence described by the general formula of a-b, where a is any integer between 1 to 560 of SEQ ID NO:70, b is an integer of 15 to 574, where both a and b correspond to the positions of nucleotide residues shown in SEQ ID NO:70, and where b is greater than or equal to a + 14.

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FEATURES OF PROTEIN ENCODED BY GENE NO: 61

This gene shares homology with the latrophilin-related protein 1 precursor as well as the calcium-independent alpha-latrotoxin receptor. alpha-Latrotoxin, a black widow spider neurotoxin, can bind to high affinity receptors on the presynaptic plasma membrane and stimulate massive neurotransmitter release in the absence of Ca2+. Neurexins, previously isolated as alpha-latrotoxin receptors, require Ca2+ for their interaction with the toxin and, thus, may not participate in the Ca2+-independent alpha-latrotoxin activity. However, latrophilin binds alpha-Latrotoxin with high affinity in the presence of various divalent cations (Ca2+, Mg2+, Ba2+, and Sr2+) as well as in EDTA. This presumably membrane-bound protein is localized to and differentially distributed among neuronal tissues, with about four times more latrophilin expressed in the cerebral cortex than in the cerebellum; subcellular fractionation showed that the protein is highly enriched in synaptosomal plasma membranes.

In specific embodiments, polypeptides of the invention comprise, or alternatively consists of, an amino acid sequence selected from the group: IYKVFRHTAGLKPEVSCFENIRSCARXXXXXXXXXXXXXWIFGVLHVVHASV

VTAYLFTVSNAFQGMFIFLFLCVLSRKIQEEYYRLFKNVPCC (SEQ ID NO:703), WIFGVLHVVHASVVTAYLFTVSNAFQGMFIFLFLCVLSRKIQEEYYRLFKNVPCC (SEQ ID NO:704), IYKVFRHTAGLKPEVSCFENIRSCAR (SEQ ID NO:705), IIYKVFRHTAGLKPEVSCFENIRSCARGALALLFLLGTTWIFGVLHVVHASVVTAYLFTVSNAFQG (SEQ ID NO:706), and/or EVSCFENIRSCARGALALLFLLGTTWIFGVLH (SEQ ID NO:707). Moreover, fragments and variants of these polypeptides (such as, for example, fragments as described herein, polypeptides at least 80%, 85%, 90%, 95%, 96%, 97%, 98%, or 99% identical to these polypeptides and polypeptides encoded by the polynucleotide which hybridizes, under stringent conditions, to the polynucleotide encoding these polypeptides) are encompassed by the invention. Antibodies that bind polypeptides of the invention are also encompassed by the invention. Polynucleotides encoding these polypeptides are also encompassed by the invention.

The translation product of this gene also shares sequence homology with CD 97, a seven transmembrane bound receptor (see Genbank Accession No. 2213659). The gene encoding the disclosed cDNA is believed to reside on chromosome 1. Accordingly, polynucleotides related to this invention are useful as a marker in linkage analysis for chromosome 1.

This gene is expressed primarily in infant brain and in endothelial cells.

Polynucleotides and polypeptides of the invention are useful as reagents for differential identification of the tissue(s) or cell type(s) present in a biological sample and for diagnosis of diseases and conditions which include, but are not limited to, neurological, vascular, and hematopoietic disorders. Similarly, polypeptides and antibodies directed to these polypeptides are useful in providing immunological probes for differential identification of the tissue(s) or cell type(s). For a number of disorders of the above tissues or cells, particularly of the neurological and hematopoietic systems, expression of this gene at significantly higher or lower levels may be routinely detected in certain tissues or cell types (e.g., vascular, neural, hematopoietic, and cancerous and wounded tissues) or bodily fluids (e.g., lymph, serum, plasma, urine, synovial fluid and spinal fluid) or another tissue or cell sample taken from an individual having such a disorder, relative to the standard gene

expression level, i.e., the expression level in healthy tissue or bodily fluid from an individual not having the disorder.

Predicted epitopes include those comprising a sequence shown in SEQ ID NO: 309 as residues: Lys-13 to Leu-21.

The tissue distribution in infant brain genes suggest that the protein product may be useful in the detection and/or treatment of neurodegenerative disease states and behavioral disorders such as Alzheimer's Disease, Parkinson's Disease, Huntington's Disease, schizophrenia, mania, dementia, paranoia, obsessive compulsive disorder and panic disorder, while its expression in hematopoietic cell types indicates that the gene could be important for the treatment or detection of immune or hematopoietic disorders including arthritis, asthma and immunodeficiency diseases. Moreover, the expression within endothelial tissue indicates that the protein product of this gene may show utility in the treatment and/or prevention of a variety of vascular disorders, which include, but are not limited to microvascular disease, atherosclerosis, stroke, embolism, and aneurysm. Furthermore, expression within infant tissue indicates that this protein may play a role in the regulation of cellular division, and may show utility in the diagnosis and treatment of cancer and other proliferative disorders. Similarly, developmental tissues rely on decisions involving cell differentiation and/or apoptosis in pattern formation. Thus, this protein may also be involved in apoptosis or tissue differentiation and could again be useful in cancer therapy. Protein, as well as, antibodies directed against the protein may show utility as a tumor marker and/or immunotherapy targets for the above listed tissues.

Many polynucleotide sequences, such as EST sequences, are publicly available and accessible through sequence databases. Some of these sequences are related to SEQ ID NO:71 and may have been publicly available prior to conception of the present invention. Preferably, such related polynucleotides are specifically excluded from the scope of the present invention. To list every related sequence is cumbersome. Accordingly, preferably excluded from the present invention are one or more polynucleotides comprising a nucleotide sequence described by the general formula of a-b, where a is any integer between 1 to 918 of SEQ ID NO:71, b is an integer of 15 to 932, where both a and b correspond to the positions of nucleotide residues shown in SEQ ID NO:71, and where b is greater than or equal to a + 14.

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FEATURES OF PROTEIN ENCODED BY GENE NO: 62

In a specific embodiment, polypeptides of the invention, comprise or alternatively consist of, one or more of the following amino acid sequences: TTILRTCTIVCFYYWFNGVMVLLFFLDRNLLTFNQASIMPFSNTDFLHCLSFK KKLMLLRYIFYVVLTGPTLSLKGDENQIKNLFT (SEQ ID NO:708), IVCFYYWFNGVMVLLFFLDRNLL (SEQ ID NO:709), and/or LLRYIFYVVLTGPTLSLKGDENQI (SEQ ID NO:710). Polynucleotides encoding these polypeptides are also encompassed by the invention as are antibodies that bind one or more of these polypeptides. Moreover, fragments and variants of these polypeptides (such as, for example, fragments as described herein, polypeptides at least 80%, 85%, 90%, 95%, 96%, 97%, 98%, or 99% identical to these polypeptides and polypeptides encoded by the polynucleotide which hybridizes, under stringent conditions, to the polynucleotide encoding these polypeptides , or the complement there of are encompassed by the invention. Antibodies that bind polypeptides of the invention are also encompassed by the invention. Polynucleotides encoding these polypeptides are also encompassed by the invention.

Also preferred are polypeptides, comprising or alternatively consisting of, the mature polypeptide which is predicted to consist of residues: PTCYSRMRALSQEITRDFNLLQVSEPSEPCVRYLPRLYLDIHNYCVLDKLRDF VASPPCWKVAQVDSLKDKARKLYTIMNSFCRRDLVFLLDDCNALEYPIPVTT VLPDRQR (SEQ ID NO:1245) of the foregoing sequence (SEQ ID NO:310), and biologically active fragments of the mature polypeptide (e.g., fragments that induce hematopoiesis). Polynucleotides encoding these polypeptides are also encompassed by the invention. Moreover, fragments and variants of these polypeptides (such as, for example, fragments as described herein, polypeptides at least 80%, 85%, 90%, 95%, 96%, 97%, 98%, or 99% identical to these polypeptides and polypeptides encoded by the polynucleotide which hybridizes, under stringent conditions, to the polynucleotide encoding these polypeptides , or the complement there of are encompassed by the invention. Antibodies that bind polypeptides of the invention are

also encompassed by the invention. Polynucleotides encoding these polypeptides are also encompassed by the invention.

Figures 5A-5B show the nucleotide (SEQ ID NO:72) and deduced amino acid sequence (SEQ ID NO:310) corresponding to this gene.

Figure 6 shows an analysis of the amino acid sequence (SEQ ID NO:310). Alpha, beta, turn and coil regions; hydrophilicity and hydrophobicity; amphipathic regions; flexible regions; antigenic index and surface probability are shown, and all were generated using the default settings of the recited computer algorithms. In the "Antigenic Index or Jameson-Wolf" graph, the positive peaks indicate locations of the highly antigenic regions of the protein, i.e., regions from which epitope-bearing peptides of the invention can be obtained. Polypeptides comprising, or alternatively consisting of, domains defined by these graphs are contemplated by the present invention, as are polynucleotides encoding these polypeptides.

The data presented in Figure 6 are also represented in tabular form in Table 5. The columns are labeled with the headings "Res", "Position", and Roman Numerals I-XIV. The column headings refer to the following features of the amino acid sequence presented in Figure 6, and Table 5: "Res": amino acid residue of SEQ ID NO:310 and Figures 5A-5B; "Position": position of the corresponding residue within SEQ ID NO:310 and Figures 5A-5B; I: Alpha, Regions - Garnier-Robson; II: Alpha, Regions - Chou-Fasman; III: Beta, Regions - Garnier-Robson; IV: Beta, Regions - Chou-Fasman; V: Turn, Regions - Garnier-Robson; VI: Turn, Regions - Chou-Fasman; VII: Coil, Regions - Garnier-Robson; VIII: Hydrophilicity Plot - Kyte-Doolittle; IX: Hydrophobicity Plot - Hopp-Woods; X: Alpha, Amphipathic Regions - Eisenberg; XI: Beta, Amphipathic Regions - Eisenberg; XII: Flexible Regions - Karplus-Schulz; XIII: Antigenic Index - Jameson-Wolf; and XIV: Surface Probability Plot - Emini.

Preferred embodiments of the invention in this regard include fragments that comprise, or alternatively consisting of, one or more of the following regions: alpha-helix and alpha-helix forming regions ("alpha-regions"), beta-sheet and beta-sheet forming regions ("beta-regions"), turn and turn-forming regions ("turn-regions"), coil and coil-forming regions ("coil-regions"), hydrophilic regions, hydrophobic regions, alpha amphipathic regions, beta amphipathic regions, flexible regions, surface-

forming regions and high antigenic index regions. The data representing the structural or functional attributes of the protein set forth in Figures 5A-5B and/or Table 5, as described above, was generated using the various modules and algorithms of the DNA*STAR set on default parameters. In a preferred embodiment, the data presented in columns VIII, IX, XIII, and XIV of Table 5 can be used to determine regions of the protein which exhibit a high degree of potential for antigenicity. Regions of high antigenicity are determined from the data presented in columns VIII, IX, XIII, and/or XIV by choosing values which represent regions of the polypeptide which are likely to be exposed on the surface of the polypeptide in an environment in which antigen recognition may occur in the process of initiation of an immune response.

Certain preferred regions in these regards are set out in Figures 5A-5B, but may, as shown in Table 5, be represented or identified by using tabular representations of the data presented in Figure 6 The DNA*STAR computer algorithm used to generate Figure 6 set on the original default parameters) was used to present the data in Figure 6 in a tabular format (See Table 5). The tabular format of the data in Figure 6 is used to easily determine specific boundaries of a preferred region.

The present invention is further directed to fragments of the polynucleotide sequences described herein. By a fragment of, for example, the polynucleotide sequence of a deposited cDNA or the nucleotide sequence shown in SEQ ID NO: 72, is intended polynucleotide fragments at least about 15nt, and more preferably at least about 20 nt, at least about 25nt, still more preferably at least about 30 nt, at least about 35nt, and even more preferably, at least about 40 nt in length, at least about 45nt in length, at least about 50nt in length, at least about 60nt in length, at least about 70nt in length, at least about 80nt in length, at least about 90nt in length, at least about 100nt in length, at least about 125nt in length, at least about 150nt in length, at least about 175nt in length, which are useful as diagnostic probes and primers as discussed herein. Of course, larger fragments 200-500 nt in length are also useful according to the present invention, as are fragments corresponding to most, if not all, of the nucleotide sequence of a deposited cDNA or as shown in SEQ ID NO:72. By a fragment at least 20 nt in length, for example, is intended fragments

which include 20 or more contiguous bases from the nucleotide sequence of a deposited cDNA or the nucleotide sequence as shown in SEQ ID NO:72. In this context "about" includes the particularly recited size, an sizes larger or smaller by several (5, 4, 3, 2, or 1) nucleotides, at either terminus or at both termini.

Representative examples of polynucleotide fragments of the invention include, for example, fragments that comprise, or alternatively, consist of, a sequence from about nucleotide 1 to about 50, from about 51 to about 100, from about 101 to about 150, from about 151 to about 200, from about 201 to about 250, from about 251 to about 300, from about 301 to about 350, from about 351 to about 400, from about 401 to about 450, from about 451 to about 500, and from about 501 to about 550, and from about 551 to about 600, from about 601 to about 650, from about 651 to about 700, from about 701 to about 750, from about 751 to about 800, from about 801 to about 850, from about 851 to about 900, from about 901 to about 950, or from about 951 to about 985 of SEQ ID NO:72, or the complementary strand thereto, or the cDNA contained in a deposited clone. In this context "about" includes the particularly recited ranges, and ranges larger or smaller by several (5, 4, 3, 2, or 1) nucleotides, at either terminus or at both termini. In additional embodiments, the polynucleotides of the invention encode functional attributes of the corresponding protein.

Preferred polypeptide fragments of the invention comprise, or alternatively consist of, the secreted protein having a continuous series of deleted residues from the amino or the carboxyl terminus, or both. Particularly, N-terminal deletions of the polypeptide can be described by the general formula m-136 where m is an integer from 2 to 136, where m corresponds to the position of the amino acid residue identified in SEQ ID NO:310. More in particular, the invention provides polynucleotides encoding polypeptides comprising, or alternatively consisting of, an amino acid sequence selected from the group: R-2 to R-136; T-3 to R-136; P-4 to R-136; G-5 to R-136; P-6 to R-136; L-7 to R-136; P-8 to R-136; V-9 to R-136; L-10 to R-136; L-11 to R-136; L-12 to R-136; L-13 to R-136; L-14 to R-136; A-15 to R-136; G-16 to R-136; A-17 to R-136; P-18 to R-136; A-19 to R-136; A-20 to R-136; R-21 to R-136; P-22 to R-136; T-23 to R-136; P-24 to R-136; P-25 to R-136; T-26 to R-136; C-27 to R-136; Y-28 to R-136; S-29 to R-136; R-30 to R-136; M-31 to R-136; R-32 to R-136; A-33 to R-136; L-34 to R-136; S-35 to R-136; Q-36 to R-136; E-37 to R-136; I-38 to R-136; T-39 to

R-136; R-40 to R-136; D-41 to R-136; F-42 to R-136; N-43 to R-136; L-44 to R-136; L-45 to R-136; Q-46 to R-136; V-47 to R-136; S-48 to R-136; E-49 to R-136; P-50 to R-136; S-51 to R-136; E-52 to R-136; P-53 to R-136; C-54 to R-136; V-55 to R-136; R-56 to R-136; Y-57 to R-136; L-58 to R-136; P-59 to R-136; R-60 to R-136; L-61 to R-136; Y-62 to R-136; L-63 to R-136; D-64 to R-136; I-65 to R-136; H-66 to R-136; N-67 to R-136; Y-68 to R-136; C-69 to R-136; V-70 to R-136; L-71 to R-136; D-72 to R-136; K-73 to R-136; L-74 to R-136; R-75 to R-136; D-76 to R-136; F-77 to R-136; V-78 to R-136; A-79 to R-136; S-80 to R-136; P-81 to R-136; P-82 to R-136; C-83 to R-136; W-84 to R-136; K-85 to R-136; V-86 to R-136; A-87 to R-136; Q-88 to R-136; V-89 to R-136; D-90 to R-136; S-91 to R-136; L-92 to R-136; K-93 to R-136; D-94 to R-136; K-95 to R-136; A-96 to R-136; R-97 to R-136; K-98 to R-136; L-99 to R-136; Y-100 to R-136; T-101 to R-136; I-102 to R-136; M-103 to R-136; N-104 to R-136; S-105 to R-136; F-106 to R-136; C-107 to R-136; R-108 to R-136; R-109 to R-136; D-110 to R-136; L-111 to R-136; V-112 to R-136; F-113 to R-136; L-114 to R-136; L-115 to R-136; D-116 to R-136; D-117 to R-136; C-118 to R-136; N-119 to R-136; A-120 to R-136; L-121 to R-136; E-122 to R-136; Y-123 to R-136; P-124 to R-136; I-125 to R-136; P-126 to R-136; V-127 to R-136; T-128 to R-136; T-129 to R-136; V-130 to R-136; and L-131 to R-136 of SEQ ID NO:310. Polypeptides encoded by these polynucleotides are also encompassed by the invention. Moreover, fragments and variants of these polypeptides (such as, for example, fragments as described herein, polypeptides at least 80%, 85%, 90%, 95%, 96%, 97%, 98%, or 99% identical to these polypeptides and polypeptides encoded by the polynucleotide which hybridizes, under stringent conditions, to the polynucleotide encoding these polypeptides, or the complement there of are encompassed by the invention. Antibodies that bind polypeptides of the invention are also encompassed by the invention. Polynucleotides encoding these polypeptides are also encompassed by the invention.

Also as mentioned above, even if deletion of one or more amino acids from the C-terminus of a protein results in modification or loss of one or more biological functions of the protein (e.g., ability to induce hematopoiesis), other functional activities (e.g., biological activities, ability to multimerize, ability to bind receptors, ability to activate receptors, ability to bind and block receptor activation, ability to

inhibit receptor activation without binding (e.g., as a dominant negative inhibitor of oligomeric complexes), ability to generate antibodies, ability to bind antibodies) may still be retained. For example the ability of the shortened polypeptide to induce and/or bind to antibodies which recognize the complete or mature forms of the polypeptide generally will be retained when less than the majority of the residues of the complete or mature polypeptide are removed from the C-terminus. Whether a particular polypeptide lacking C-terminal residues of a complete polypeptide retains such immunologic activities can readily be determined by routine methods described herein and otherwise known in the art. It is not unlikely that a polypeptide with a large number of deleted C-terminal amino acid residues may retain some biological or immunogenic activities. In fact, peptides composed of as few as six amino acid residues may often evoke an immune response.

Accordingly, the present invention further provides polypeptides having one or more residues deleted from the carboxyl terminus of the amino acid sequence of the polypeptide shown in Figures 5A-5B (SEQ ID NO:310), as described by the general formula 1-n, where n is an integer from 6 to 135, where n corresponds to the position of the amino acid residue identified in SEQ ID NO:310. More in particular, the invention provides polynucleotides encoding polypeptides comprising, or alternatively consisting of, an amino acid sequence selected from the group: M-1 to Q-135; M-1 to R-134; M-1 to D-133; M-1 to P-132; M-1 to L-131; M-1 to V-130; M-1 to T-129; M-1 to T-128; M-1 to V-127; M-1 to P-126; M-1 to I-125; M-1 to P-124; M-1 to Y-123; M-1 to E-122; M-1 to L-121; M-1 to A-120; M-1 to N-119; M-1 to C-118; M-1 to D-117; M-1 to D-116; M-1 to L-115; M-1 to L-114; M-1 to F-113; M-1 to V-112; M-1 to L-111; M-1 to D-110; M-1 to R-109; M-1 to R-108; M-1 to C-107; M-1 to F-106; M-1 to S-105; M-1 to N-104; M-1 to M-103; M-1 to I-102; M-1 to T-101; M-1 to Y-100; M-1 to L-99; M-1 to K-98; M-1 to R-97; M-1 to A-96; M-1 to K-95; M-1 to D-94; M-1 to K-93; M-1 to L-92; M-1 to S-91; M-1 to D-90; M-1 to V-89; M-1 to Q-88; M-1 to A-87; M-1 to V-86; M-1 to K-85; M-1 to W-84; M-1 to C-83; M-1 to P-82; M-1 to P-81; M-1 to S-80; M-1 to A-79; M-1 to V-78; M-1 to F-77; M-1 to D-76; M-1 to R-75; M-1 to L-74; M-1 to K-73; M-1 to D-72; M-1 to L-71; M-1 to V-70; M-1 to C-69; M-1 to Y-68; M-1 to N-67; M-1 to H-66; M-1 to I-65; M-1 to D-64; M-1 to L-63; M-1 to Y-62; M-1 to L-61; M-1 to R-60; M-1 to P-59; M-1 to L-58;

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M-1 to Y-57; M-1 to R-56; M-1 to V-55; M-1 to C-54; M-1 to P-53; M-1 to E-52; M-1 to S-51; M-1 to P-50; M-1 to E-49; M-1 to S-48; M-1 to V-47; M-1 to Q-46; M-1 to L-45; M-1 to L-44; M-1 to N-43; M-1 to F-42; M-1 to D-41; M-1 to R-40; M-1 to T-39; M-1 to I-38; M-1 to E-37; M-1 to Q-36; M-1 to S-35; M-1 to L-34; M-1 to A-33; M-1 to R-32; M-1 to M-31; M-1 to R-30; M-1 to S-29; M-1 to Y-28; M-1 to C-27; M-1 to T-26; M-1 to P-25; M-1 to P-24; M-1 to T-23; M-1 to P-22; M-1 to R-21; M-1 to A-20; M-1 to A-19; M-1 to P-18; M-1 to A-17; M-1 to G-16; M-1 to A-15; M-1 to L-14; M-1 to L-13; M-1 to L-12; M-1 to L-11; M-1 to L-10; M-1 to V-9; M-1 to P-8; and M-1 to L-7 of SEQ ID NO:310. Polypeptides encoded by these polynucleotides are also encompassed by the invention. Moreover, fragments and variants of these polypeptides (such as, for example, fragments as described herein, polypeptides at least 80%, 85%, 90%, 95%, 96%, 97%, 98%, or 99% identical to these polypeptides and polypeptides encoded by the polynucleotide which hybridizes, under stringent conditions, to the polynucleotide encoding these polypeptides, or the complement there of are encompassed by the invention. Antibodies that bind polypeptides of the invention are also encompassed by the invention. Polynucleotides encoding these polypeptides are also encompassed by the invention.

In addition, any of the above listed N- or C-terminal deletions can be combined to produce a N- and C-terminal deleted polypeptide. The invention also provides polypeptides comprising, or alternatively consisting of, one or more amino acids deleted from both the amino and the carboxyl termini, which may be described generally as having residues m-n of SEQ ID NO:310, where n and m are integers as described above. More in particular, the invention provides polynucleotides encoding polypeptides comprising, or alternatively consisting of, an amino acid sequence selected from the group: M-1 to A-15; R-2 to G-16; T-3 to A-17; P-4 to P-18; G-5 to A-19; P-6 to A-20; L-7 to R-21; P-8 to P-22; V-9 to T-23; L-10 to P-24; L-11 to P-25; L-12 to T-26; L-13 to C-27; L-14 to Y-28; A-15 to S-29; G-16 to R-30; A-17 to M-31; P-18 to R-32; A-19 to A-33; A-20 to L-34; R-21 to S-35; P-22 to Q-36; T-23 to E-37; P-24 to I-38; P-25 to T-39; T-26 to R-40; C-27 to D-41; Y-28 to F-42; S-29 to N-43; R-30 to L-44; M-31 to L-45; R-32 to Q-46; A-33 to V-47; L-34 to S-48; S-35 to E-49; Q-36 to P-50; E-37 to S-51; I-38 to E-52; T-39 to P-53; R-40 to C-54; D-41 to V-55; F-42 to R-56; N-43 to Y-57; L-44 to L-58; L-45 to P-59; Q-

46 to R-60; V-47 to L-61; S-48 to Y-62; E-49 to L-63; P-50 to D-64; S-51 to I-65; E-52 to H-66; P-53 to N-67; C-54 to Y-68; V-55 to C-69; R-56 to V-70; Y-57 to L-71; L-58 to D-72; P-59 to K-73; R-60 to L-74; L-61 to R-75; Y-62 to D-76; L-63 to F-77; D-64 to V-78; I-65 to A-79; H-66 to S-80; N-67 to P-81; Y-68 to P-82; C-69 to C-83; V-70 to W-84; L-71 to K-85; D-72 to V-86; K-73 to A-87; L-74 to Q-88; R-75 to V-89; D-76 to D-90; F-77 to S-91; V-78 to L-92; A-79 to K-93; S-80 to D-94; P-81 to K-95; P-82 to A-96; C-83 to R-97; W-84 to K-98; K-85 to L-99; V-86 to Y-100; A-87 to T-101; Q-88 to I-102; V-89 to M-103; D-90 to N-104; S-91 to S-105; L-92 to F-106; K-93 to C-107; D-94 to R-108; K-95 to R-109; A-96 to D-110; R-97 to L-111; K-98 to V-112; L-99 to F-113; Y-100 to L-114; T-101 to L-115; I-102 to D-116; M-103 to D-117; N-104 to C-118; S-105 to N-119; F-106 to A-120; C-107 to L-121; R-108 to E-122; R-109 to Y-123; D-110 to P-124; L-111 to I-125; V-112 to P-126; F-113 to V-127; L-114 to T-128; L-115 to T-129; D-116 to V-130; D-117 to L-131; C-118 to P-132; N-119 to D-133; A-120 to R-134; L-121 to Q-135; and E-122 to R-136 of SEQ ID NO:310. Polynucleotides encoding these polypeptides are also encompassed by the invention. Moreover, fragments and variants of these polypeptides (such as, for example, fragments as described herein, polypeptides at least 80%, 85%, 90%, 95%, 96%, 97%, 98%, or 99% identical to these polypeptides and polypeptides encoded by the polynucleotide which hybridizes, under stringent conditions, to the polynucleotide encoding these polypeptides , or the complement there of are encompassed by the invention. Antibodies that bind polypeptides of the invention are also encompassed by the invention. Polynucleotides encoding these polypeptides are also encompassed by the invention.

The present invention is also directed to proteins containing polypeptides at least 80%, 85%, 90%, 92%, 93%, 94%, 95%, 96%, 97%, 98% or 99% identical to a polypeptide sequence set forth herein as m-n. In preferred embodiments, the application is directed to proteins containing polypeptides at least 80%, 85%, 90%, 95%, 96%, 97%, 98% or 99% identical to polypeptides having the amino acid sequence of the specific N- and C-terminal deletions recited herein. Polynucleotides encoding these polypeptides are also encompassed by the invention.

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Also included are polynucleotide sequences encoding a polypeptide consisting of a portion of the complete amino acid sequence encoded by a cDNA clone contained in ATCC Deposit No. 97975 (deposited April 4, 1997) and ATCC Deposit No. 209081 (deposited May 29, 1997), where this portion excludes any integer of amino acid residues from 1 to about 606 (end of protein minus six) amino acids from the amino terminus of the complete amino acid sequence encoded by a cDNA clone contained in ATCC Deposit No. 97975 and 209081, or any integer of amino acid residues from 6 to about 612 amino acids from the carboxyl terminus, or any combination of the above amino terminal and carboxyl terminal deletions, of the complete amino acid sequence encoded by the cDNA clone contained in ATCC Deposit No. 97975 and 209081. Polypeptides encoded by these polynucleotides also are encompassed by the invention. Moreover, fragments and variants of these polypeptides (such as, for example, fragments as described herein, polypeptides at least 80%, 85%, 90%, 95%, 96%, 97%, 98%, or 99% identical to these polypeptides and polypeptides encoded by the polynucleotide which hybridizes, under stringent conditions, to the polynucleotide encoding these polypeptides, or the complement there of are encompassed by the invention. Antibodies that bind polypeptides of the invention are also encompassed by the invention. Polynucleotides encoding these polypeptides are also encompassed by the invention.

The gene encoding the disclosed cDNA is believed to reside on chromosome 4. Accordingly, polynucleotides related to this invention have uses that include, but are not limited to, serving as probes or primers in chromosome identification, chromosome mapping, and linkage analysis for chromosome 4.

This gene is expressed primarily in fetal liver and fetal spleen.

Polynucleotides and polypeptides of the invention are useful as reagents for differential identification of the tissue(s) or cell type(s) present in a biological sample and for diagnosis of diseases and conditions which include, but are not limited to, hematopoietic, immunological, developmental, and/or hepatic disorders. Similarly, polypeptides and antibodies directed to these polypeptides are useful in providing immunological probes for differential identification of the tissue(s) or cell type(s). For a number of disorders of the above tissues or cells, particularly of the immune and hematopoetic systems, expression of this gene at significantly higher or lower levels

may be routinely detected in certain tissues or cell types (e.g., hematopoietic, immune, hepatic, developmental, and cancerous and wounded tissues) or bodily fluids (e.g., lymph, amniotic fluid, bile, serum, plasma, urine, synovial fluid and spinal fluid) or another tissue or cell sample taken from an individual having such a disorder, relative to the standard gene expression level, i.e., the expression level in healthy tissue or bodily fluid from an individual not having the disorder. For example, polynucleotides and polypeptides of the invention, polynucleotide and polypeptide fragments, and polynucleotide and polypeptide variants, and antibodies directed to these polypeptides are useful for identifying, selecting, targeting and/or stimulating proliferation of hematopoietic stem cells (a.k.a., hematopoietic progenitor cells).

Cytokines typically exert their respective biochemical and physiological effects by binding to specific receptor molecules. Receptor binding then stimulates specific signal transduction pathways (Kishimoto, T., *et al., Cell* **76:**253-262 (1994)). The specific interactions of cytokines with their receptors are often the primary regulators of a wide variety of cellular processes including activation, proliferation, and differentiation (Arai, K. -I, *et al., Ann. Rev. Biochem.* **59:**783-836 (1990); Paul, W. E. and Seder, R. A., *Cell* **76:**241-251 (1994)).

The polynucleotides and polypeptides of this invention may be useful for the diagnosis and treatment of a variety of immune system and hematopoietic disorders, pathologies, and/or deficiencies. For example, this gene and/or gene product may play a role in regulating the proliferation; survival; differentiation; and/or activation of hematopoietic cell lineages, including blood stem cells. Furthermore, polypeptides of this invention may be involved in the regulation of cytokine production, antigen presentation, or other processes useful for treatment of cancer, particularly leukemia (e.g., by boosting immune responses, suppressing hyperproliferative activity, or enhancing recovery of healthy hematopoietic cell populations during or following chemotherapy). Moreover, the polynucleotides and polypeptides of this invention, as well as antibodies against the polypeptides of this invention, may be useful for treating immunological and hematopoietic disorders; such as for examples, arthritis, asthma, immunodeficiency diseases (e.g. AIDS), leukemia, rheumatoid arthritis, granulomatous disease, inflammatory bowel disease, sepsis, acne, neutropenia,

neutrophilia, psoriasis, hypersensitivities, such as T-cell mediated cytotoxicity; immune reactions to transplanted organs and tissues, such as host-versus-graft and graft-versus-host diseases, or autoimmunity disorders, demyelination, systemic lupus erythematosis, drug induced hemolytic anemia, rheumatoid arthritis, Sjogren's disease, and scleroderma. Moreover, the polypeptide of this invention represents a secreted factor that is likely to have activity in stimulating the differentiation of blood cells, or recruiting immune and hematopoietic cells to sites of injury. Thus, this polypeptide is thought to be useful in the expansion of stem cells and committed progenitors of various blood lineages, and in the differentiation and/or proliferation of various cell types.

Preferred polypeptides of the present invention comprise, or alternatively consist of, one or more of the immunogenic epitopes shown in SEQ ID NO: 310 as residues: Met-1 to Leu-7, Pro-18 to Cys-27, Ser-29 to Ser-35, Glu-37 to Asp-41, Gln-46 to Cys-54, Asp-72 to Val-78, Pro-81 to Trp-84, Ser-91 to Lys-98, Asn-104 to Leu-111, Asp-116 to Leu-121, and Val-130 to Arg-136. Polynucleotides encoding said polypeptides are also encompassed by the invention. Antibodies that bind said epitopes or other polypeptides of the invention are also encompassed.

The tissue distribution of this gene in fetal liver and spleen indicates that the gene could be important for the treatment or detection of immune or hematopoietic disorders including arthritis, leukemia, and immunodeficiency diseases. Moreover, the protein product of this gene is useful for the treatment and diagnosis of hematopoetic related disorders such as anemia, pancytopenia, leukopenia, thrombocytopenia or leukemia since stromal cells are important in the production of cells of hematopoietic lineages. The uses include bone marrow cell ex vivo culture, bone marrow transplantation, bone marrow reconstitution, radiotherapy or chemotherapy of neoplasia. The gene product may also be involved in lymphopoiesis, therefore, it can be used in immune disorders such as infection, inflammation, allergy, immunodeficiency etc. In addition, this gene product may have commercial utility in the expansion of stem cells and committed progenitors of various blood lineages, and in the differentiation and/or proliferation of various cell types. Moreover, expression within fetal tissue indicates that this protein may play a role in the regulation of cellular division, and may show utility in the diagnosis and

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treatment of cancer and other proliferative disorders. Similarly, developmental tissues rely on decisions involving cell differentiation and/or apoptosis in pattern formation. Thus, this protein may also be involved in apoptosis or tissue differentiation and could again be useful in cancer therapy. Protein, as well as, antibodies directed against the protein may show utility as a tumor marker and/or immunotherapy targets for the above listed tissues.

Many polynucleotide sequences, such as EST sequences, are publicly available and accessible through sequence databases. Some of these sequences are related to SEQ ID NO:72 and may have been publicly available prior to conception of the present invention. Preferably, such related polynucleotides are specifically excluded from the scope of the present invention. To list every related sequence is cumbersome. Accordingly, preferably excluded from the present invention are one or more polynucleotides comprising a nucleotide sequence described by the general formula of a-b, where a is any integer between 1 to 982 of SEQ ID NO:72, b is an integer of 15 to 996, where both a and b correspond to the positions of nucleotide residues shown in SEQ ID NO:72, and where b is greater than or equal to a + 14.

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FEATURES OF PROTEIN ENCODED BY GENE NO: 63

This gene shares homology with human serum amyloid protein (See Genbank Accession No. W13671).

In specific embodiments, polypeptides of the invention comprise, or alternatively consists of, an amino acid sequence selected from the group: ALTRIPPGDWVINVTAVSFAGKTTARFFHSSPPSLGDQARTDPGHQRRD (SEQ ID NO:711), SMLLLFPLQERPQQDSFIRLLLAWGTRLELTLDIKGGI (SEQ ID NO:712), TGLWADGFSSHIIPPLMSRVSSSLVPQARRRRMKESCCGLSCKGNSSNIDYPV TGRNSCERAPLCAFALHFQERTXITGXGEDPGPFQSXGRVTASRXTLACSHV AMTPAGCXQALGTPSSYCVRKAPRA (SEQ ID NO:713), and/or QARRRRMKESCCGLSCKGNSSNIDYPVT (SEQ ID NO:714). Moreover, fragments and variants of these polypeptides (such as, for example, fragments as

described herein, polypeptides at least 80%, 85%, 90%, 95%, 96%, 97%, 98%, or 99% identical to these polypeptides and polypeptides encoded by the polynucleotide which hybridizes, under stringent conditions, to the polynucleotide encoding these polypeptides) are encompassed by the invention. Antibodies that bind polypeptides of the invention are also encompassed by the invention. Polynucleotides encoding these polypeptides are also encompassed by the invention.

The gene encoding the disclosed cDNA is believed to reside on chromosome 9. Accordingly, polynucleotides related to this invention are useful as a marker in linkage analysis for chromosome 9.

This gene is expressed primarily in fetal liver and spleen.

Polynucleotides and polypeptides of the invention are useful as reagents for differential identification of the tissue(s) or cell type(s) present in a biological sample and for diagnosis of diseases and conditions which include, but are not limited to, hematopoietic, immune, and/or developmental disorders. Similarly, polypeptides and antibodies directed to these polypeptides are useful in providing immunological probes for differential identification of the tissue(s) or cell type(s). For a number of disorders of the above tissues or cells, particularly of the hematopoietic and immune systems, expression of this gene at significantly higher or lower levels may be routinely detected in certain tissues or cell types (e.g., hematopoietic, immune, developmental, and cancerous and wounded tissues) or bodily fluids (e.g., lymph, amniotic fluid, serum, plasma, urine, synovial fluid and spinal fluid) or another tissue or cell sample taken from an individual having such a disorder, relative to the standard gene expression level, i.e., the expression level in healthy tissue or bodily fluid from an individual not having the disorder.

The tissue distribution of this gene in fetal liver-spleen indicates that the gene is important for the treatment or detection of immune or hematopoietic disorders including arthritis, leukemia, and immunodeficiency diseases. Moreover, the protein product of this gene is useful for the treatment and diagnosis of hematopoetic related disorders such as anemia, pancytopenia, leukopenia, thrombocytopenia or leukemia since stromal cells are important in the production of cells of hematopoietic lineages. The uses include bone marrow cell ex vivo culture, bone marrow transplantation, bone marrow reconstitution, radiotherapy or chemotherapy of neoplasia. The gene

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product may also be involved in lymphopoiesis, therefore, it can be used in immune disorders such as infection, inflammation, allergy, immunodeficiency, etc. In addition, this gene product may have commercial utility in the expansion of stem cells and committed progenitors of various blood lineages, and in the differentiation and/or proliferation of various cell types. Furthermore, expression within fetal tissue indicates that this protein may play a role in the regulation of cellular division, and may show utility in the diagnosis and treatment of cancer and other proliferative disorders. Similarly, developmental tissues rely on decisions involving cell differentiation and/or apoptosis in pattern formation. Thus, this protein may also be involved in apoptosis or tissue differentiation and could again be useful in cancer therapy. Protein, as well as, antibodies directed against the protein may show utility as a tumor marker and/or immunotherapy targets for the above listed tissues.

Many polynucleotide sequences, such as EST sequences, are publicly available and accessible through sequence databases. Some of these sequences are related to SEQ ID NO:73 and may have been publicly available prior to conception of the present invention. Preferably, such related polynucleotides are specifically excluded from the scope of the present invention. To list every related sequence is cumbersome. Accordingly, preferably excluded from the present invention are one or more polynucleotides comprising a nucleotide sequence described by the general formula of a-b, where a is any integer between 1 to 771 of SEQ ID NO:73, b is an integer of 15 to 785, where both a and b correspond to the positions of nucleotide residues shown in SEQ ID NO:73, and where b is greater than or equal to a + 14.

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FEATURES OF PROTEIN ENCODED BY GENE NO: 64

In specific embodiments, polypeptides of the invention comprise, or alternatively consists of, the following amino acid sequence: LWRSSGVER (SEQ ID NO:715). Moreover, fragments and variants of this polypeptide (such as, for example, fragments as described herein, polypeptides at least 80%, 85%, 90%, 95%, 96%, 97%, 98%, or 99% identical to these polypeptides and polypeptides encoded by the polynucleotide which hybridize, under stringent conditions, to the polynucleotide

encoding this polypeptide are encompassed by the invention. Antibodies that bind polypeptides of the invention are also encompassed by the invention. Polynucleotides encoding this polypeptide are also encompassed by the invention.

The gene encoding the disclosed cDNA is believed to reside on chromosome 3. Accordingly, polynucleotides related to this invention are useful as a marker in linkage analysis for chromosome 3.

This gene is expressed specifically in the brain.

Polynucleotides and polypeptides of the invention are useful as reagents for differential identification of the tissue(s) or cell type(s) present in a biological sample and for diagnosis of diseases and conditions which include, but are not limited to, neural disorders, particularly neurodegenerative disease states. Similarly, polypeptides and antibodies directed to these polypeptides are useful in providing immunological probes for differential identification of the tissue(s) or cell type(s). For a number of disorders of the above tissues or cells, particularly of the neurological systems, expression of this gene at significantly higher or lower levels may be routinely detected in certain tissues or cell types (e.g., neural, and cancerous and wounded tissues) or bodily fluids (e.g., lymph, serum, plasma, urine, synovial fluid and spinal fluid) or another tissue or cell sample taken from an individual having such a disorder, relative to the standard gene expression level, i.e., the expression level in healthy tissue or bodily fluid from an individual not having the disorder.

The tissue distribution in brain indicates that the protein product of this gene is useful for the detection/treatment of neurodegenerative disease states, behavioral disorders, or inflammatory conditions such as Alzheimer's Disease, Parkinson's Disease, Huntington's Disease, Tourette's Syndrome, meningitis, encephalitis, demyelinating diseases, peripheral neuropathies, neoplasia, trauma, congenital malformations, spinal cord injuries, ischemia and infarction, aneurysms, hemorrhages, schizophrenia, mania, dementia, paranoia, obsessive compulsive disorder, panic disorder, learning disabilities, ALS, psychoses, autism, and altered behaviors, including disorders in feeding, sleep patterns, balance, and perception. In addition, elevated expression of this gene product in regions of the brain indicates that it plays a role in normal neural function. Potentially, this gene product is involved in synapse formation, neurotransmission, learning, cognition, homeostasis, or neuronal

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differentiation or survival. Moreover, the gene or gene product may also play a role in the treatment and/or detection of developmental disorders associated with the developing embryo, sexually-linked disorders, or disorders of the cardiovascular system. Protein, as well as, antibodies directed against the protein may show utility as a tumor marker and/or immunotherapy targets for the above listed tissues.

Many polynucleotide sequences, such as EST sequences, are publicly available and accessible through sequence databases. Some of these sequences are related to SEQ ID NO:74 and may have been publicly available prior to conception of the present invention. Preferably, such related polynucleotides are specifically excluded from the scope of the present invention. To list every related sequence is cumbersome. Accordingly, preferably excluded from the present invention are one or more polynucleotides comprising a nucleotide sequence described by the general formula of a-b, where a is any integer between 1 to 1055 of SEQ ID NO:74, b is an integer of 15 to 1069, where both a and b correspond to the positions of nucleotide residues shown in SEQ ID NO:74, and where b is greater than or equal to a + 14.

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FEATURES OF PROTEIN ENCODED BY GENE NO: 65

This gene shares homology with a yeast protein.

In specific embodiments, polypeptides of the invention comprise, or alternatively consists of, the following amino acid sequence: LQEVNITLPENSVWYERYKFDIPVFHL (SEQ ID NO:716). Moreover, fragments and variants of this polypeptide (such as, for example, fragments as described herein, polypeptides at least 80%, 85%, 90%, 95%, 96%, 97%, 98%, or 99% identical to these polypeptides and polypeptides encoded by the polynucleotide which hybridize, under stringent conditions, to the polynucleotide encoding this polypeptide are encompassed by the invention. Antibodies that bind polypeptides of the invention are also encompassed by the invention. Polynucleotides encoding this polypeptide are also encompassed by the invention. (See Genbank Accession No. 1332638).

This gene is expressed primarily in fetal tissue (fetus and fetal liver).

Polynucleotides and polypeptides of the invention are useful as reagents for differential identification of the tissue(s) or cell type(s) present in a biological sample and for diagnosis of diseases and conditions which include, but are not limited to, hepatic, developmental, immune, and/or hematopoietic disorders, including cancers (e.g. hepatoblastoma). Similarly, polypeptides and antibodies directed to these polypeptides are useful in providing immunological probes for differential identification of the tissue(s) or cell type(s). For a number of disorders of the above tissues or cells, particularly of the hepatic system, expression of this gene at significantly higher or lower levels may be routinely detected in certain tissues or cell types (e.g., hepatic, developmental, immune, hematopoietic, and cancerous and wounded tissues) or bodily fluids (e.g., lymph, amniotic fluid, bile, serum, plasma, urine, synovial fluid and spinal fluid) or another tissue or cell sample taken from an individual having such a disorder, relative to the standard gene expression level, i.e., the expression level in healthy tissue or bodily fluid from an individual not having the disorder.

Predicted epitopes include those comprising a sequence shown in SEQ ID NO: 313 as residues: Asn-72 to Glu-77.

The tissue distribution in fetal liver indicates that the protein product of this gene is useful for the detection and treatment of liver disorders and cancers (e.g. hepatoblastoma, jaundice, hepatitis, liver metabolic diseases and conditions that are attributable to the differentiation of hepatocyte progenitor cells). In addition the expression in fetus would suggest a useful role for the protein product in developmental abnormalities, fetal deficiencies, pre-natal disorders and various would-healing models and/or tissue trauma. Moreover, the protein product of this gene is useful for the treatment and diagnosis of hematopoetic related disorders such as anemia, pancytopenia, leukopenia, thrombocytopenia or leukemia since stromal cells are important in the production of cells of hematopoietic lineages. The uses include bone marrow cell ex vivo culture, bone marrow transplantation, bone marrow reconstitution, radiotherapy or chemotherapy of neoplasia. The gene product may also be involved in lymphopoiesis, therefore, it can be used in immune disorders such as infection, inflammation, allergy, immunodeficiency etc. In addition, this gene product may have commercial utility in the expansion of stem cells and committed

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progenitors of various blood lineages, and in the differentiation and/or proliferation of various cell types. Protein, as well as, antibodies directed against the protein may show utility as a tumor marker and/or immunotherapy targets for the above listed tissues.

Many polynucleotide sequences, such as EST sequences, are publicly available and accessible through sequence databases. Some of these sequences are related to SEQ ID NO:75 and may have been publicly available prior to conception of the present invention. Preferably, such related polynucleotides are specifically excluded from the scope of the present invention. To list every related sequence is cumbersome. Accordingly, preferably excluded from the present invention are one or more polynucleotides comprising a nucleotide sequence described by the general formula of a-b, where a is any integer between 1 to 817 of SEQ ID NO:75, b is an integer of 15 to 831, where both a and b correspond to the positions of nucleotide residues shown in SEQ ID NO:75, and where b is greater than or equal to a + 14.

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FEATURES OF PROTEIN ENCODED BY GENE NO: 66

This gene has homology with a B-cell surface antigen which may indicate that this gene plays a role in the immune response, including, but not limited to disorders and infections of the immune system.

Preferred polynucleotide fragments comprise the following sequence: GTAGCATGTAGCCAGTCGAATAACNTATAAGGACAAAGTGGAGTCCACGC GTGCGCCGTCTAGACTAGTGGATCCCCCGGCTGCAGGATTCGGCACGAG (SEQ ID NO:718). Also preferred are polypeptides comprising polypeptide fragments encoded by these polynucleotide fragments.

This gene shares homology with an interferon-gamma receptor (See Genbank Accession No.T94535).

In specific embodiments, polypeptides of the invention comprise, or alternatively consists of, an amino acid sequence selected from the group: MQGSGSQFRACLLCLCFSCPCSPGGPRWNSRQGGRRFPKTCRAISQNLVFKY KTFCPVRYMQPHRSSLCLHFTSYVFILSTWGSLRTYSTDLKKKKKNSRGGPVP

IRPKS (SEQ ID NO:717),
MQGSGSQFRACLLCLCFSCPCSPGGPRWNSRQGGRRFPKTCRAISQNLVFK (SEQ ID NO:719),
PVRYMQPHRSSLCLHFTSYVFILSTWGSLRTYSTDLKKKKKNSRGGPVPIRPK S (SEQ ID NO:720),
GEEQRDCSLGWRGVGMRATHCQAARMFVLFSLPKYAGL (SEQ ID NO:721),
TSGSPGCRIRHELPGEEQRDCSLGWRGVGMRATHCQAAR (SEQ ID NO:722),
EPPIAKQQECSCFFPFQNMQGSGSQFRACLLCLCFSCPCSPGGPRWNSRQGGR RFPKTCRAISQNLVFKYKTFCPVRYMQPHRSSLCLHFTSYVFILSTWGSLRTY STDLKKKKKNSRGGPVPIRPKS (SEQ ID NO:723), and/or
QFRACLLCLCFSCPCSPGGPRWNSRQGGRRF (SEQ ID NO:724). Moreover, fragments and variants of these polypeptides (such as, for example, fragments as described herein, polypeptides at least 80%, 85%, 90%, 95%, 96%, 97%, 98%, or 99% identical to these polypeptides and polypeptides encoded by the polynucleotide which hybridizes, under stringent conditions, to the polynucleotide encoding these polypeptides) are encompassed by the invention. Antibodies that bind polypeptides of the invention are also encompassed by the invention. Polynucleotides encoding these polypeptides are also encompassed by the invention.

This gene is expressed primarily in T-cells and gall bladder.

Polynucleotides and polypeptides of the invention are useful as reagents for differential identification of the tissue(s) or cell type(s) present in a biological sample and for diagnosis of diseases and conditions which include, but are not limited to, immunological disorders and conditions (immunodeficiencies, cancer, leukemia, hematopoiesis), in addition to metabolic, gastrointestinal, and/or digestive disorders. Similarly, polypeptides and antibodies directed to these polypeptides are useful in providing immunological probes for differential identification of the tissue(s) or cell type(s). For a number of disorders of the above tissues or cells, particularly of the immune and digestive systems, expression of this gene at significantly higher or lower levels may be routinely detected in certain tissues or cell types (e.g., immune, hematopoietic, metabolic, gastrointestinal, digestive, and cancerous and wounded tissues) or bodily fluids (e.g., lymph, serum, bile, plasma, urine, synovial fluid and spinal fluid) or another tissue or cell sample taken from an individual having such a

disorder, relative to the standard gene expression level, i.e., the expression level in healthy tissue or bodily fluid from an individual not having the disorder.

Predicted epitopes include those comprising a sequence shown in SEQ ID NO: 314 as residues: Thr-41 to Gly-52.

The tissue distribution in T-cells indicates that the protein product of this gene is useful for the treatment and diagnosis of immune disorders including: leukemias, lymphomas, auto-immune disorders, immunosuppressive (transplantation) and immunodeficiencies (e.g. AIDS), inflammation and hematopoietic disorders. Moreover, the expression of this gene in gall bladder would suggest a possible role for this gene product in digestive disorders, particularly of the pancreas or liver. Protein, as well as, antibodies directed against the protein may show utility as a tumor marker and/or immunotherapy targets for the above listed tissues.

Many polynucleotide sequences, such as EST sequences, are publicly available and accessible through sequence databases. Some of these sequences are related to SEQ ID NO:76 and may have been publicly available prior to conception of the present invention. Preferably, such related polynucleotides are specifically excluded from the scope of the present invention. To list every related sequence is cumbersome. Accordingly, preferably excluded from the present invention are one or more polynucleotides comprising a nucleotide sequence described by the general formula of a-b, where a is any integer between 1 to 576 of SEQ ID NO:76, b is an integer of 15 to 590, where both a and b correspond to the positions of nucleotide residues shown in SEQ ID NO:76, and where b is greater than or equal to a + 14.

FEATURES OF PROTEIN ENCODED BY GENE NO: 67

In specific embodiments, polypeptides of the invention comprise, or alternatively consists of, an amino acid sequence selected from the group: NQFTSCILFCDGGHWRELLFQSI (SEQ ID NO:725), AMSSKLLNLLALLQYSVHDHCHPRRLLKRGARATLRHKGWGPSSLRGCESF QIVLIGWGPDLAVGFGRGKLLSRSLPVRHGGVSEFCLPHRDVVRLEKVKK (SEQ ID NO:726), and/or GPSSLRGCESFQIVLIGWGPDLAVGFGRGKLLS (SEQ

ID NO:727). Moreover, fragments and variants of these polypeptides (such as, for example, fragments as described herein, polypeptides at least 80%, 85%, 90%, 95%, 96%, 97%, 98%, or 99% identical to these polypeptides and polypeptides encoded by the polynucleotide which hybridizes, under stringent conditions, to the polynucleotide encoding these polypeptides) are encompassed by the invention. Antibodies that bind polypeptides of the invention are also encompassed by the invention. Polynucleotides encoding these polypeptides are also encompassed by the invention.

The gene encoding the disclosed cDNA is believed to reside on chromosome 11. Accordingly, polynucleotides related to this invention are useful as a marker in linkage analysis for chromosome 11.

This gene is expressed primarily in a variety of fetal and developmental tissues (e.g. fetal spleen, infant brain).

Polynucleotides and polypeptides of the invention are useful as reagents for differential identification of the tissue(s) or cell type(s) present in a biological sample and for diagnosis of diseases and conditions which include, but are not limited to, developmental, immune or neurological abnormalities. Similarly, polypeptides and antibodies directed to these polypeptides are useful in providing immunological probes for differential identification of the tissue(s) or cell type(s). For a number of disorders of the above tissues or cells, particularly of the developing immune and central nervous systems, expression of this gene at significantly higher or lower levels may be routinely detected in certain tissues or cell types (e.g., neural, immune, hematopoietic, hepatic, developmental, and cancerous and wounded tissues) or bodily fluids (e.g., lymph, amniotic fluid, bile, serum, plasma, urine, synovial fluid and spinal fluid) or another tissue or cell sample taken from an individual having such a disorder, relative to the standard gene expression level, i.e., the expression level in healthy tissue or bodily fluid from an individual not having the disorder.

Predicted epitopes include those comprising a sequence shown in SEQ ID NO: 315 as residues: Ser-38 to Ser-43.

The tissue distribution in fetal tissues indicates that the protein product of this gene is useful for developmental abnormalities or fetal deficiencies. The detection in infant brain would suggest a role in neurological disorders (both developmental and neurodegenerative conditions of the brain and nervous system, behavioral disorders,

depression, schizophrenia, Alzheimer's disease, Parkinson's disease, Huntington's disease, mania, dementia). In addition, the detection in spleen would similarly suggest a role in the detection and treatment of immune disorders (e.g. immunodeficiency, inflammation, cancer, wound healing, tissue repair, hematopoiesis). Protein, as well as, antibodies directed against the protein may show utility as a tumor marker and/or immunotherapy targets for the above listed tissues.

Many polynucleotide sequences, such as EST sequences, are publicly available and accessible through sequence databases. Some of these sequences are related to SEQ ID NO:77 and may have been publicly available prior to conception of the present invention. Preferably, such related polynucleotides are specifically excluded from the scope of the present invention. To list every related sequence is cumbersome. Accordingly, preferably excluded from the present invention are one or more polynucleotides comprising a nucleotide sequence described by the general formula of a-b, where a is any integer between 1 to 1260 of SEQ ID NO:77, b is an integer of 15 to 1274, where both a and b correspond to the positions of nucleotide residues shown in SEQ ID NO:77, and where b is greater than or equal to a + 14.

FEATURES OF PROTEIN ENCODED BY GENE NO: 68

In specific embodiments, polypeptides of the invention comprise, or alternatively consists of, the following amino acid sequence: TRKNIDFXETEKYYLFSFSNNVSFKNFWLKYN (SEQ ID NO:728). Moreover, fragments and variants of this polypeptide (such as, for example, fragments as described herein, polypeptides at least 80%, 85%, 90%, 95%, 96%, 97%, 98%, or 99% identical to these polypeptides and polypeptides encoded by the polynucleotide which hybridize, under stringent conditions, to the polynucleotide encoding this polypeptide are encompassed by the invention. Antibodies that bind polypeptides of the invention are also encompassed by the invention. Polynucleotides encoding this polypeptide are also encompassed by the invention.

This gene is expressed primarily in spleen, T-cells, and fetal heart.

Polynucleotides and polypeptides of the invention are useful as reagents for differential identification of the tissue(s) or cell type(s) present in a biological sample and for diagnosis of diseases and conditions which include, but are not limited to, immunological or hematopoietic deficiencies or disorders, including AIDS and cardiovascular or developmental conditions. Similarly, polypeptides and antibodies directed to these polypeptides are useful in providing immunological probes for differential identification of the tissue(s) or cell type(s). For a number of disorders of the above tissues or cells, particularly of the immune and cardiovascular systems, expression of this gene at significantly higher or lower levels may be routinely detected in certain tissues or cell types (e.g., immune, hematopoietic, cardiovascular, developmental, and cancerous and wounded tissues) or bodily fluids (e.g., lymph, amniotic fluid, serum, plasma, urine, synovial fluid and spinal fluid) or another tissue or cell sample taken from an individual having such a disorder, relative to the standard gene expression level, i.e., the expression level in healthy tissue or bodily fluid from an individual not having the disorder.

The tissue distribution in spleen and T-cells indicates that the protein product of this gene is useful for the diagnosis and treatment of immune disorders including: leukemias, lymphomas, autoimmune disorders, immunodeficiencies (e.g. AIDS), immunosuppressive conditions (transplantation) and hematopoietic disorders. Moreover, the expression in fetal heart indicates that the protein product of this gene is useful for the treatment and diagnosis of cardiovascular disorders (e.g. heart disease, restenosis, atherosclerosis, stoke, angina, thrombosis). Protein, as well as, antibodies directed against the protein may show utility as a tumor marker and/or immunotherapy targets for the above listed tissues.

Many polynucleotide sequences, such as EST sequences, are publicly available and accessible through sequence databases. Some of these sequences are related to SEQ ID NO:78 and may have been publicly available prior to conception of the present invention. Preferably, such related polynucleotides are specifically excluded from the scope of the present invention. To list every related sequence is cumbersome. Accordingly, preferably excluded from the present invention are one or more polynucleotides comprising a nucleotide sequence described by the general formula of a-b, where a is any integer between 1 to 1119 of SEQ ID NO:78, b is an

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integer of 15 to 1133, where both a and b correspond to the positions of nucleotide residues shown in SEQ ID NO:78, and where b is greater than or equal to a + 14.

FEATURES OF PROTEIN ENCODED BY GENE NO: 69

This gene shares homology with a human collagen protein.

In specific embodiments, polypeptides of the invention comprise, or alternatively consists of, an amino acid sequence selected from the group:

MPRKTSKCRQLLCSGASRNADTAARQSTCSSHRPPGKIPSLGPRRXPGCXSVP SSRGEQSTGSPAAPRCGRRDAHRGLPGGAAMTPGDTWASFNPRAGHSKSQG EGQESSGASRQDRHPVSHWVERQREAWGAPRSSSAGGVKVAATTEREPEFKI KTGKA (SEQ ID NO:729),

CSGASRNADTAARQSTCSSHRPPGKIPSLGPRRXPGCXSVPSSRGEQSTGSPA APRCGRRDAHRGLPGGAAMTPGDTWASFNPRAGHS (SEQ ID NO:730),

QGEGQESSGASRQDRHPVSHWVERQREAWGAPRSSSAGGVKVAATTEREPE FKIKTGKA (SEQ ID NO:731),

IRHEGKRMLNESRKPLSFASRLSSLYFKLGFPFCGRSNLYSTCTAAPGGSPGLP LPFYPVADG (SEQ ID NO:732),

TRAESLFPLLHAFPVFILNSGSLSVVAATFTPPALLLLGAPQASLCLSTQWLTG CLSCLDAPLLSCPSPWLLLCPALGLKLAHVSPGVMAAPPGRPLCASRLPHLGA AGEPVLCSPRLLGTELQPGXLRGPRLGILPGGRWEEQVLCLAAVSAFLDAPEH RSCRHFEVFLGMCQIT (SEQ ID NO:733),

PALGLKLAHVSPGVMAAPPGRPLCASRLP (SEQ ID NO:734),

GGRWEEQVLCLAAVSAFLDAPEHR (SEQ ID NO:735),

SWPMCPPESWLLLLGGLCVRHVFHTWGQLASPCSVPLGCLAQSCSLGXSVDP DWGFCQGGDGRSRCFAWRLCLHFWTPQSTEVAGTLRSSSACARLHE (SEQ ID NO:736), and/or GDGRSRCFAWRLCLHFWTPQSTEVAGTLR (SEQ ID NO:737). Moreover, fragments and variants of these polypeptides (such as, for example, fragments as described herein, polypeptides at least 80%, 85%, 90%, 95%, 96%, 97%, 98%, or 99% identical to these polypeptides and polypeptides encoded by the polynucleotide which hybridizes, under stringent conditions, to the polynucleotide

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encoding these polypeptides) are encompassed by the invention. Antibodies that bind polypeptides of the invention are also encompassed by the invention. Polynucleotides encoding these polypeptides are also encompassed by the invention.

This gene is expressed primarily in fetal heart.

Polynucleotides and polypeptides of the invention are useful as reagents for differential identification of the tissue(s) or cell type(s) present in a biological sample and for diagnosis of diseases and conditions which include, but are not limited to, cardiovascular or developmental disorders, particularly vascular conditions. Similarly, polypeptides and antibodies directed to these polypeptides are useful in providing immunological probes for differential identification of the tissue(s) or cell type(s). For a number of disorders of the above tissues or cells, particularly of the cardiovascular system, expression of this gene at significantly higher or lower levels may be routinely detected in certain tissues or cell types (e.g., cardiovascular, developmental, skeletal, vascular, and cancerous and wounded tissues) or bodily fluids (e.g., lymph, amniotic fluid, serum, plasma, urine, synovial fluid and spinal fluid) or another tissue or cell sample taken from an individual having such a disorder, relative to the standard gene expression level, i.e., the expression level in healthy tissue or bodily fluid from an individual not having the disorder.

Predicted epitopes include those comprising a sequence shown in SEQ ID NO: 317 as residues: Pro-32 to Ser-39.

The tissue distribution in fetal heart indicates that the protein product of this gene is useful for the treatment and diagnosis of cardiovascular disorders (e.g. heart disease, restenosis, atherosclerosis, stroke, angina, thrombosis), in addition to vascular disorders, such as microvascular disease. Expression within fetal tissue indicates that this protein may play a role in the regulation of cellular division, and may show utility in the diagnosis and treatment of cancer and other proliferative disorders. Similarly, developmental tissues rely on decisions involving cell differentiation and/or apoptosis in pattern formation. Thus this protein may also be involved in apoptosis or tissue differentiation and could again be useful in cancer therapy. Protein, as well as, antibodies directed against the protein may show utility as a tumor marker and/or immunotherapy targets for the above listed tissues.

Many polynucleotide sequences, such as EST sequences, are publicly available and accessible through sequence databases. Some of these sequences are related to SEQ ID NO:79 and may have been publicly available prior to conception of the present invention. Preferably, such related polynucleotides are specifically excluded from the scope of the present invention. To list every related sequence is cumbersome. Accordingly, preferably excluded from the present invention are one or more polynucleotides comprising a nucleotide sequence described by the general formula of a-b, where a is any integer between 1 to 647 of SEQ ID NO:79, b is an integer of 15 to 661, where both a and b correspond to the positions of nucleotide residues shown in SEQ ID NO:79, and where b is greater than or equal to a + 14.

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FEATURES OF PROTEIN ENCODED BY GENE NO: 70

The translation product of this gene shares sequence homology with a chicken single-strand DNA-binding protein. The promoter region of the chicken alpha2(I) collagen gene contains a pyrimidine-rich element that is well conserved in different mammalian species. This sequence can also form an unusual DNA structure as shown by its sensitivity to SI nuclease in vitro and it lies in a region that is DNase I-hypersensitive only when this promoter is active. The high affinity of this protein for this conserved pyrimidine-rich region indicates that it might be involved in the transcriptional regulation of the alpha2(I) collagen gene.

In specific embodiments, polypeptides of the invention comprise, or alternatively consists of, an amino acid sequence selected from the group:
MSPRYPGGPRPPLRIPNQALGGVPGSQPLLPSGMDPTRQQGHPNMGGPMQR MTPPRGMVPLGPQNYGGAMRPPLNALGGPGMPGMNMGPGGGRPWPNPTN ANSIPYSSASPGNYVGPPGGGGPPGTPIMPSPADSTNSGDNMYTLMNAVPPGP NRPNFPMGPGSDGPMGGLGGMESHHMNGSLGSGDMDSISKNSPNNMSLSNQ PGTPRDDGEMGGNFLNPFQSESYSPSMTMSV (SEQ ID NO:738),
MSPRYPGGPRPPLRIPNQALGGVPGSQPLLPSGMDPTRQQGHPNMGGPMQR MTPPRGMVPLGPQNYGGAMRPPLNALGGPGMPGMNMGPGGGRPWPNPTN ANSIPYSSASPGNY (SEQ ID NO:739),

LNALGGPGMPGMNMGPGGGRPWPNPTNANSIPYSSASPGNYVGPPGGGGPP GTPIMPSPADSTNSGDNMYTLMNAVPPGPN (SEQ ID NO:740), GPMGGLGGMESHHMNGSLGSGDMDSISKNSPNNMSLSNQPGTPRDDGEMG GNFLNPFQSESYSPSMTMSV (SEQ ID NO:741), TCEHSSEAKAFHDY (SEQ ID NO:742), and/or RRETCEHSSEAKAFHDYPF (SEQ ID NO:743),. Moreover, fragments and variants of these polypeptides (such as, for example, fragments as described herein, polypeptides at least 80%, 85%, 90%, 95%, 96%, 97%, 98%, or 99% identical to these polypeptides and polypeptides encoded by the polynucleotide which hybridizes, under stringent conditions, to the polynucleotide encoding these polypeptides) are encompassed by the invention. Antibodies that bind polypeptides of the invention are also encompassed by the invention. Polynucleotides encoding these polypeptides are also encompassed by the invention. (See Genbank Accession No. 1562534)

This gene is expressed primarily in placenta, and to a lesser extent, in fetal heart.

Polynucleotides and polypeptides of the invention are useful as reagents for differential identification of the tissue(s) or cell type(s) present in a biological sample and for diagnosis of diseases and conditions which include, but are not limited to, developmental abnormalities, fetal deficiencies, and particularly of the cardiovascular system and/or vascular conditions. Similarly, polypeptides and antibodies directed to these polypeptides are useful in providing immunological probes for differential identification of the tissue(s) or cell type(s). For a number of disorders of the above tissues or cells, particularly of the reproductive system, expression of this gene at significantly higher or lower levels may be routinely detected in certain tissues or cell types (e.g., developmental, vascular, cardiovascular, reproductive, and cancerous and wounded tissues) or bodily fluids (e.g., lymph, amniotic fluid, serum, plasma, urine, synovial fluid and spinal fluid) or another tissue or cell sample taken from an individual having such a disorder, relative to the standard gene expression level, i.e., the expression level in healthy tissue or bodily fluid from an individual not having the disorder.

Predicted epitopes include those comprising a sequence shown in SEQ ID NO: 318 as residues: Met-1 to Leu-13, Gly-33 to Gly-46, Pro-48 to Gly-57, Pro-63 to

Gly-68, Pro-89 to Asn-102, Ser-108 to Asn-113, Pro-118 to Pro-124, Pro-132 to Asn-141, Pro-151 to Asn-157, Ile-191 to Met-199, Ser-202 to Gly-215, Phe-222 to Pro-229.

The tissue distribution in fetal heart and placenta indicates that the protein product of this gene is useful for the detection and treatment of developmental abnormalities or fetal deficiencies, ovarian and other endometrial cancers, reproductive dysfunction, cardiovascular disorders, and pre-natal disorders, in particular vascular disorders, which include, but are not limited to, stroke, angina, microvascular disease, atherosclerosis, embolism, and aneurysm. Protein, as well as, antibodies directed against the protein may show utility as a tumor marker and/or immunotherapy targets for the above listed tissues.

Many polynucleotide sequences, such as EST sequences, are publicly available and accessible through sequence databases. Some of these sequences are related to SEQ ID NO:80 and may have been publicly available prior to conception of the present invention. Preferably, such related polynucleotides are specifically excluded from the scope of the present invention. To list every related sequence is cumbersome. Accordingly, preferably excluded from the present invention are one or more polynucleotides comprising a nucleotide sequence described by the general formula of a-b, where a is any integer between 1 to 1364 of SEQ ID NO:80, b is an integer of 15 to 1378, where both a and b correspond to the positions of nucleotide residues shown in SEQ ID NO:80, and where b is greater than or equal to a + 14.

FEATURES OF PROTEIN ENCODED BY GENE NO: 71

In specific embodiments, polypeptides of the invention comprise, or alternatively consists of, an amino acid sequence selected from the group: TITLFQSAWCFFSKYCTDFT (SEQ ID NO:744), VRGCEDGGGGGIWGGWWPGQQMAPPWLSCPHRQFPHFHSGRQRRQSDLLK EELPQPSGAAGRASGNKPYTPPPASNSLTLRLLSFRFNAFNRSHPQPSLNYKD RQ (SEQ ID NO:745), PWLSCPHRQFPHFHSGRQRRQSDLL (SEQ ID NO:746), and/or RLLSFRFNAFNRSHPQPSLN (SEQ ID NO:747). Moreover, fragments and

variants of these polypeptides (such as, for example, fragments as described herein, polypeptides at least 80%, 85%, 90%, 95%, 96%, 97%, 98%, or 99% identical to these polypeptides and polypeptides encoded by the polynucleotide which hybridizes, under stringent conditions, to the polynucleotide encoding these polypeptides) are encompassed by the invention. Antibodies that bind polypeptides of the invention are also encompassed by the invention. Polynucleotides encoding these polypeptides are also encompassed by the invention.

The gene encoding the disclosed cDNA is believed to reside on chromosome 7. Accordingly, polynucleotides related to this invention are useful as a marker in linkage analysis for chromosome 7.

This gene is expressed primarily in fetal liver, and to a lesser extent, in the breast and testes.

Polynucleotides and polypeptides of the invention are useful as reagents for differential identification of the tissue(s) or cell type(s) present in a biological sample and for diagnosis of diseases and conditions which include, but are not limited to, hepatic disorders (including hepatoblastomas), hematopoietic, immune, and/or reproductive disorders. Similarly, polypeptides and antibodies directed to these polypeptides are useful in providing immunological probes for differential identification of the tissue(s) or cell type(s). For a number of disorders of the above tissues or cells, particularly of the hepatic and reproductive systems, expression of this gene at significantly higher or lower levels may be routinely detected in certain tissues or cell types (e.g., hematopoietic, immune, hepatic, reproductive, developmental, and cancerous and wounded tissues) or bodily fluids (e.g., lymph, amniotic fluid, bile, serum, plasma, urine, synovial fluid and spinal fluid) or another tissue or cell sample taken from an individual having such a disorder, relative to the standard gene expression level, i.e., the expression level in healthy tissue or bodily fluid from an individual not having the disorder.

The tissue distribution in fetal liver indicates that the protein product of this gene is useful for the detection and treatment of liver disorders and cancers (e.g. hepatoblastoma, jaundice, hepatitis, liver metabolic diseases and conditions that are attributable to the differentiation of hepatocyte progenitor cells). The expression in testes and breast indicates that the protein product of this gene is useful for the

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detection and treatment of endocrine and reproductive disorders (e.g. sperm maturation, milk production, testicular and breast cancers). Protein, as well as, antibodies directed against the protein may show utility as a tumor marker and/or immunotherapy targets for the above listed tissues.

Many polynucleotide sequences, such as EST sequences, are publicly available and accessible through sequence databases. Some of these sequences are related to SEQ ID NO:81 and may have been publicly available prior to conception of the present invention. Preferably, such related polynucleotides are specifically excluded from the scope of the present invention. To list every related sequence is cumbersome. Accordingly, preferably excluded from the present invention are one or more polynucleotides comprising a nucleotide sequence described by the general formula of a-b, where a is any integer between 1 to 1426 of SEQ ID NO:81, b is an integer of 15 to 1440, where both a and b correspond to the positions of nucleotide residues shown in SEQ ID NO:81, and where b is greater than or equal to a + 14.

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FEATURES OF PROTEIN ENCODED BY GENE NO: 72

In specific embodiments, polypeptides of the invention comprise, or alternatively consists of, an amino acid sequence selected from the group: RDSSLWAAALSFRQQCSSLASCLVSMYSRPGRQHRAKAGAGSQTEQCWGRK VDAVV (SEQ ID NO:748), CLVSMYSRPGRQHRAKAGAGSQTEQCW (SEQ ID NO:749), PEHGFSSCDFWEGAPSSGPKEGGRSPPQLACVWGMNLSSPPCLALLTNRACL AVNWHRVTLFPGIQVCNQNTGEEKLQDPCPHLSS (SEQ ID NO:750), RSPPQLACVWGMNLSSPPCLALLTNRACLA (SEQ ID NO:751), CERDSETSSIAMTCIKHKPPKQKKRLSLLPGFRSALPRVCRCHMITVQREAFRT HTGCSTSVHLPSRGGFLPDF (SEQ ID NO:752), and/or KKRLSLLPGFRSALPRVCRCHMITVQRE (SEQ ID NO:753).

Moreover, fragments and variants of these polypeptides (such as, for example, fragments as described herein, polypeptides at least 80%, 85%, 90%, 95%, 96%, 97%, 98%, or 99% identical to these polypeptides and polypeptides encoded by the

polynucleotide which hybridizes, under stringent conditions, to the polynucleotide encoding these polypeptides) are encompassed by the invention. Antibodies that bind polypeptides of the invention are also encompassed by the invention. Polynucleotides encoding these polypeptides are also encompassed by the invention.

The gene encoding the disclosed cDNA is believed to reside on chromosome 1. Accordingly, polynucleotides related to this invention are useful as a marker in linkage analysis for chromosome 1.

This gene is expressed primarily in smooth muscle, and to a lesser extent, in brain.

Polynucleotides and polypeptides of the invention are useful as reagents for differential identification of the tissue(s) or cell type(s) present in a biological sample and for diagnosis of diseases and conditions which include, but are not limited to, cardiovascular and neurological disorders, particularly embolism, atherosclerosis, stroke, aneurysm, and microvascular disease. Similarly, polypeptides and antibodies directed to these polypeptides are useful in providing immunological probes for differential identification of the tissue(s) or cell type(s). For a number of disorders of the above tissues or cells, particularly of the cardiovascular and central nervous systems, expression of this gene at significantly higher or lower levels may be routinely detected in certain tissues or cell types (e.g., neural, vascular, endothelial, smooth muscle, and cancerous and wounded tissues) or bodily fluids (e.g., lymph, serum, plasma, urine, synovial fluid and spinal fluid) or another tissue or cell sample taken from an individual having such a disorder, relative to the standard gene expression level, i.e., the expression level in healthy tissue or bodily fluid from an individual not having the disorder.

The tissue distribution in brain and smooth muscle indicates that the protein product of this gene is useful for the detection and treatment of restenosis, atherosclerosis, stroke, angina, thrombosis, wound healing and other conditions of heart disease. Moreover, the protein product of this gene is useful for the detection and treatment of developmental, degenerative and behavioral conditions of the brain and nervous system (e.g. schizophrenia, depression, Alzheimer's disease, Parkinson's disease, Huntington's disease, mania, dementia, paranoia, addictive behavior and

sleep disorders). Protein, as well as, antibodies directed against the protein may show utility as a tumor marker and/or immunotherapy targets for the above listed tissues.

Many polynucleotide sequences, such as EST sequences, are publicly available and accessible through sequence databases. Some of these sequences are related to SEQ ID NO:82 and may have been publicly available prior to conception of the present invention. Preferably, such related polynucleotides are specifically excluded from the scope of the present invention. To list every related sequence is cumbersome. Accordingly, preferably excluded from the present invention are one or more polynucleotides comprising a nucleotide sequence described by the general formula of a-b, where a is any integer between 1 to 1367 of SEQ ID NO:82, b is an integer of 15 to 1381, where both a and b correspond to the positions of nucleotide residues shown in SEQ ID NO:82, and where b is greater than or equal to a + 14.

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FEATURES OF PROTEIN ENCODED BY GENE NO: 73

This gene shares homology with human stromalin-2, which is believed to play an integral role in modulating cellular function of hematopoietic cells and tissues, and may possibly serve as a tumor suppressor.

In specific embodiments, polypeptides of the invention comprise, or alternatively consists of, an amino acid sequence selected from the group: QAFVLLSDLLLIFSPQMIVGGRDFLRPLVFFPEATLQSELASFLMDHVFIQPGD LGSGA (SEQ ID NO:754), ACSYLLCNPEFTFFSRADFARSQLVDLLTDRFQQELEELLQVG (SEQ ID NO:755), QKQLSSLRDRMVAFCELCQSCLSDVDTEIQEQVST (SEQ ID NO:756), QVILPALTLVYFSILWTLTHISKSDAS (SEQ ID NO:757), STHDLTRWELYEPCCQLLQKAVDTGXVPHQV (SEQ ID NO:758), TSFLFPLQAFVLLSDLLLIFSPQMIVGGRDFLRPLVFFPEATLQSELASFLMDH VFIQ PGDLGSGA (SEQ ID NO:759), GWGACSYLLCNPEFTFFSRADFARSQLVDLLTDRFQQELEELLQVGAGAGQ WDTPNKGGRGCKTGDVD (SEQ ID NO:760), VWVLDGIMGTEESVSSFFPFKPLCPQKQLSSLRDRMVAFCELCQSCLSDVDTE

IQEQVSTDSSGSNKASIPAPIPRRN (SEQ ID NO:761), NASLPSTSEWLSSSSPSRFYWCLWSWFPLFFSSITFPFLPQSTHDLTRWELYEP CCQLLQKAVDTGXVPHQVSGQARDGLGAGGLXFKDLRSRWPLGVSSLSAW SGQSEEDQVGGGHLLHSSLRRWTLLPGSSWISWKPRIILRDSRRRRVN (SEQ ID NO:762), VLGEMLLWIFFPSQSSFLDEDEVYNLAATLKRLSAFYK (SEQ ID NO:763), PKPHFSNPLLLQVILPALTLVYFSILWTLTHISKSDASPGECGS (SEQ ID NO:764), and/or HCQFLLG (SEQ ID NO:765). Moreover, fragments and variants of these polypeptides (such as, for example, fragments as described herein, polypeptides at least 80%, 85%, 90%, 95%, 96%, 97%, 98%, or 99% identical to these polypeptides and polypeptides encoded by the polynucleotide which hybridizes, under stringent conditions, to the polynucleotide encoding these polypeptides) are encompassed by the invention. Antibodies that bind polypeptides of the invention are also encompassed by the invention. Polynucleotides encoding these polypeptides are also encompassed by the invention. (See Genbank Accession No.R65208)

The gene encoding the disclosed cDNA is believed to reside on chromosome 7. Accordingly, polynucleotides related to this invention are useful as a marker in linkage analysis for chromosome 7.

This gene is expressed primarily in the brain (infant brain, adult brain, pituitary, cerebellum, hippocampus, schizophrenic hypothalamus, amygdala).

Polynucleotides and polypeptides of the invention are useful as reagents for differential identification of the tissue(s) or cell type(s) present in a biological sample and for diagnosis of diseases and conditions which include, but are not limited to, developmental disorders and neurodegenerative diseases of the brain and nervous system, in addition to immune or hematopoietic disorders. Similarly, polypeptides and antibodies directed to these polypeptides are useful in providing immunological probes for differential identification of the tissue(s) or cell type(s). For a number of disorders of the above tissues or cells, particularly of the central nervous system, expression of this gene at significantly higher or lower levels may be routinely detected in certain tissues or cell types (e.g., neural, developmental, immune, hematopoietic, and cancerous and wounded tissues) or bodily fluids (e.g., lymph, amniotic fluid, serum, plasma, urine, synovial fluid and spinal fluid) or another tissue or cell sample taken from an individual having such a disorder, relative to the

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standard gene expression level, i.e., the expression level in healthy tissue or bodily fluid from an individual not having the disorder.

Predicted epitopes include those comprising a sequence shown in SEQ ID NO: 321 as residues: Thr-25 to Lys-36, Lys-55 to Ser-63.

The tissue distribution primarily in brain, combined with the homology to the highly conserved SA-1 and SA-2 proteins, indicates that the protein product of this gene is useful for the detection and treatment of developmental, degenerative and behavioral conditions of the brain and nervous system (e.g. schizophrenia, depression, Alzheimer's disease, Parkinson's disease, Huntington's disease, mania, dementia, paranoia, addictive behavior and sleep disorders). Moreover, the protein product of this gene is useful for the treatment and diagnosis of hematopoetic related disorders such as anemia, pancytopenia, leukopenia, thrombocytopenia or leukemia since stromal cells are important in the production of cells of hematopoietic lineages. The uses include bone marrow cell ex vivo culture, bone marrow transplantation, bone marrow reconstitution, radiotherapy or chemotherapy of neoplasia. The gene product may also be involved in lymphopoiesis, therefore, it can be used in immune disorders such as infection, inflammation, allergy, immunodeficiency etc. In addition, this gene product may have commercial utility in the expansion of stem cells and committed progenitors of various blood lineages, and in the differentiation and/or proliferation of various cell types. Protein, as well as, antibodies directed against the protein may show utility as a tumor marker and/or immunotherapy targets for the above listed tissues.

Many polynucleotide sequences, such as EST sequences, are publicly available and accessible through sequence databases. Some of these sequences are related to SEQ ID NO:83 and may have been publicly available prior to conception of the present invention. Preferably, such related polynucleotides are specifically excluded from the scope of the present invention. To list every related sequence is cumbersome. Accordingly, preferably excluded from the present invention are one or more polynucleotides comprising a nucleotide sequence described by the general formula of a-b, where a is any integer between 1 to 1692 of SEQ ID NO:83, b is an integer of 15 to 1706, where both a and b correspond to the positions of nucleotide residues shown in SEQ ID NO:83, and where b is greater than or equal to a + 14.

FEATURES OF PROTEIN ENCODED BY GENE NO: 74

In specific embodiments, polypeptides of the invention comprise, or alternatively consists of, an amino acid sequence selected from the group: EFGTSLVALELHELLYHWETRAQPSLILYVVSDLRWMEFRTSCLLFDFVLFLE (SEQ ID NO:766), TKPGMVGHVPIVPATKXAEAGGSPEPGSSTLQWPMITPCTPSWATEPDHVSE DE (SEQ ID NO:767), and/or LLYHWETRAQPSLILYVVSDLRWMEFRTSC (SEQ ID NO:768).

Moreover, fragments and variants of these polypeptides (such as, for example, fragments as described herein, polypeptides at least 80%, 85%, 90%, 95%, 96%, 97%, 98%, or 99% identical to these polypeptides and polypeptides encoded by the polynucleotide which hybridizes, under stringent conditions, to the polynucleotide encoding these polypeptides) are encompassed by the invention. Antibodies that bind polypeptides of the invention are also encompassed by the invention. Polynucleotides encoding these polypeptides are also encompassed by the invention.

This gene is expressed primarily in the hypothalamus of a human suffering from schizophrenia.

Polynucleotides and polypeptides of the invention are useful as reagents for differential identification of the tissue(s) or cell type(s) present in a biological sample and for diagnosis of diseases and conditions which include, but are not limited to, disorders of the CNS, particularly schizophrenia. Similarly, polypeptides and antibodies directed to these polypeptides are useful in providing immunological probes for differential identification of the tissue(s) or cell type(s). For a number of disorders of the above tissues or cells, particularly of the CNS, such as schizophrenia expression of this gene at significantly higher or lower levels may be routinely detected in certain tissues or cell types (e.g., neural, and cancerous and wounded tissues) or bodily fluids (e.g., lymph, serum, plasma, urine, synovial fluid and spinal fluid) or another tissue or cell sample taken from an individual having such a

disorder, relative to the standard gene expression level, i.e., the expression level in healthy tissue or bodily fluid from an individual not having the disorder.

Predicted epitopes include those comprising a sequence shown in SEQ ID NO: 322 as residues: Gly-38 to Ala-44.

The tissue distribution in the hypothalamus indicates that the protein products of this gene are useful for the study, diagnosis and treatment of schizophrenia and other disorders involving the CNS. Moreover, the protein product of this gene is useful for the detection/treatment of neurodegenerative disease states, behavioral disorders, or inflammatory conditions such as Alzheimer's Disease, Parkinson's Disease, Huntington's Disease, Tourette's Syndrome, meningitis, encephalitis, demyelinating diseases, peripheral neuropathies, neoplasia, trauma, congenital malformations, spinal cord injuries, ischemia and infarction, aneurysms, hemorrhages, mania, dementia, paranoia, obsessive compulsive disorder, panic disorder, learning disabilities, ALS, psychoses, autism, and altered behaviors, including disorders in feeding, sleep patterns, balance, and perception. In addition, elevated expression of this gene product in regions of the brain indicates that it plays a role in normal neural function. Potentially, this gene product is involved in synapse formation, neurotransmission, learning, cognition, homeostasis, or neuronal differentiation or survival. Moreover, the gene or gene product may also play a role in the treatment and/or detection of developmental disorders associated with the developing embryo, sexually-linked disorders, or disorders of the cardiovascular system. Protein, as well as, antibodies directed against the protein may show utility as a tumor marker and/or immunotherapy targets for the above listed tissues.

Many polynucleotide sequences, such as EST sequences, are publicly available and accessible through sequence databases. Some of these sequences are related to SEQ ID NO:84 and may have been publicly available prior to conception of the present invention. Preferably, such related polynucleotides are specifically excluded from the scope of the present invention. To list every related sequence is cumbersome. Accordingly, preferably excluded from the present invention are one or more polynucleotides comprising a nucleotide sequence described by the general formula of a-b, where a is any integer between 1 to 559 of SEQ ID NO:84, b is an

integer of 15 to 573, where both a and b correspond to the positions of nucleotide residues shown in SEQ ID NO:84, and where b is greater than or equal to a + 14.

FEATURES OF PROTEIN ENCODED BY GENE NO: 75

In specific embodiments, polypeptides of the invention comprise, or alternatively consists of, an amino acid sequence selected from the group: LAVSTSFICCADISTALPLGSSRPAPAPRHREHEHGHQARPPRLLXTSLMPLST PAAAQLLWTQLTPMGGRPGGRHSPPTLHTGPRALPPGPPHPSLHVAALSLLR (SEQ ID NO:769), APAVPHQPPGTESTSMGTKPGLPGCSXRPLCHYQHQLXPSYFGHSSPPWG AVLVGVTPHPRCTPAPGPCRLGLHTHPCTWQLCLC (SEQ ID NO:770), CADISTALPLGSSRPAPAPRHREHEHGH (SEQ ID NO:771), WTQLTPMGGRPGGRHSPPTLHTGPR (SEQ ID NO:772), and/or HQPPGTEST SMGTKPGLPGC (SEQ ID NO:773). Moreover, fragments and variants of these polypeptides (such as, for example, fragments as described herein, polypeptides at least 80%, 85%, 90%, 95%, 96%, 97%, 98%, or 99% identical to these polypeptides and polypeptides encoded by the polynucleotide which hybridizes, under stringent conditions, to the polynucleotide encoding these polypeptides) are encompassed by the invention. Antibodies that bind polypeptides of the invention are also encompassed by the invention. Polynucleotides encoding these polypeptides are also encompassed by the invention.

This gene is expressed primarily in endometrial tumors, and to a lesser extent, in amniotic cells.

Polynucleotides and polypeptides of the invention are useful as reagents for differential identification of the tissue(s) or cell type(s) present in a biological sample and for diagnosis of diseases and conditions which include, but are not limited to, reproductive, developmental, and immune disorders, particularly cancers of those systems. Similarly, polypeptides and antibodies directed to these polypeptides are useful in providing immunological probes for differential identification of the tissue(s) or cell type(s). For a number of disorders of the above tissues or cells,

particularly of the reproductive and immune systems, expression of this gene at significantly higher or lower levels may be routinely detected in certain tissues or cell types (e.g., developmental, reproductive, and cancerous and wounded tissues) or bodily fluids (e.g., lymph, amniotic fluid, serum, plasma, urine, synovial fluid and spinal fluid) or another tissue or cell sample taken from an individual having such a disorder, relative to the standard gene expression level, i.e., the expression level in healthy tissue or bodily fluid from an individual not having the disorder.

Predicted epitopes include those comprising a sequence shown in SEQ ID NO: 323 as residues: Ser-3 to Arg-9.

The tissue distribution in endometrium and amniotic cells indicates that the protein products of this gene are useful for the study and treatment of developmental, reproductive, and immune disorders, particularly cancers of those systems. Moreover, the expression within embryonic tissue and other cellular sources marked by proliferating cells indicates that this protein may play a role in the regulation of cellular division, and may show utility in the diagnosis and treatment of cancer and other proliferative disorders. Similarly, developmental tissues rely on decisions involving cell differentiation and/or apoptosis in pattern formation. Thus this protein may also be involved in apoptosis or tissue differentiation and could again be useful in cancer therapy. Protein, as well as, antibodies directed against the protein may show utility as a tumor marker and/or immunotherapy targets for the above listed tissues.

Many polynucleotide sequences, such as EST sequences, are publicly available and accessible through sequence databases. Some of these sequences are related to SEQ ID NO:85 and may have been publicly available prior to conception of the present invention. Preferably, such related polynucleotides are specifically excluded from the scope of the present invention. To list every related sequence is cumbersome. Accordingly, preferably excluded from the present invention are one or more polynucleotides comprising a nucleotide sequence described by the general formula of a-b, where a is any integer between 1 to 670 of SEQ ID NO:85, b is an integer of 15 to 684, where both a and b correspond to the positions of nucleotide residues shown in SEQ ID NO:85, and where b is greater than or equal to a + 14.

FEATURES OF PROTEIN ENCODED BY GENE NO: 76

In specific embodiments, polypeptides of the invention comprise, or alternatively consists of, an amino acid sequence selected from the group: SRGSLLPPHLPHRVVVRVHRGAKSLKALRQYIGAAHLQLPWDGKDPARPLGI TLCLQMEIQVLG (SEQ ID NO:774), CCSFGFYYMVGSDTAEKQGPIPGSQTQEGPWLSRHTHSPRAVPESSTAPAQ PLLLPLPAPQARRWASNANGWGWDHQREGQANYPYSARPAPHNLHPQYLN LHLQTQCYAQGSGWVLPIPG QLKVGGPYILPEGLQGLCSSVHPHNNPVR (SEQ ID NO:775), HRGAKSLKALRQYIGAAHLQLPWDG (SEQ ID NO:776), PAPQARRWASNANGWGWDHQR (SEQ ID NO:777), and/or HPQYLNLHLQTQCYAQGSGWVLP (SEQ ID NO:778).

Moreover, fragments and variants of these polypeptides (such as, for example, fragments as described herein, polypeptides at least 80%, 85%, 90%, 95%, 96%, 97%, 98%, or 99% identical to these polypeptides and polypeptides encoded by the polynucleotide which hybridizes, under stringent conditions, to the polynucleotide encoding these polypeptides) are encompassed by the invention. Antibodies that bind polypeptides of the invention are also encompassed by the invention. Polynucleotides encoding these polypeptides are also encompassed by the invention.

The gene encoding the disclosed cDNA is believed to reside on chromosome 22. Accordingly, polynucleotides related to this invention are useful as a marker in linkage analysis for chromosome 22.

This gene is expressed primarily in kidney cortex, and to a lesser extent, in early stage human brain.

Polynucleotides and polypeptides of the invention are useful as reagents for differential identification of the tissue(s) or cell type(s) present in a biological sample and for diagnosis of diseases and conditions which include, but are not limited to, renal disorders such as renal cancer, developmental, or neural disorders, particularly cancers. Similarly, polypeptides and antibodies directed to these polypeptides are useful in providing immunological probes for differential identification of the tissue(s) or cell type(s). For a number of disorders of the above tissues or cells,

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particularly of the kidney expression of this gene at significantly higher or lower levels may be routinely detected in certain tissues or cell types (e.g., developmental, neural, renal, urogenital, endothelial, vascular, and cancerous and wounded tissues) or bodily fluids (e.g., lymph, serum, plasma, urine, synovial fluid and spinal fluid) or another tissue or cell sample taken from an individual having such a disorder, relative to the standard gene expression level, i.e., the expression level in healthy tissue or bodily fluid from an individual not having the disorder.

Predicted epitopes include those comprising a sequence shown in SEQ ID NO: 324 as residues: Gly-38 to Gly-45, Gly-47 to Gly-52, Pro-92 to Lys-110.

The tissue distribution in kidney cortex indicates that the protein products of this gene are useful for the study, treatment and diagnosis of renal diseases, including renal failure, nephritus, renal tubular acidosis, proteinuria, pyuria, edema, pyelonephritis, hydronephritis, nephrotic syndrome, crush syndrome, glomerulonephritis, hematuria, renal colic and kidney stones, in addition to Wilms Tumor Disease, and congenital kidney abnormalities such as horseshoe kidney, polycystic kidney, and Falconi's syndrome. Moreover, the expression within human brain indicates that the protein product of this gene is useful for the detection/treatment of neurodegenerative disease states, behavioral disorders, or inflammatory conditions such as Alzheimer's Disease, Parkinson's Disease, Huntington's Disease, Tourette's Syndrome, meningitis, encephalitis, demyelinating diseases, peripheral neuropathies, neoplasia, trauma, congenital malformations, spinal cord injuries, ischemia and infarction, aneurysms, hemorrhages, schizophrenia, mania, dementia, paranoia, obsessive compulsive disorder, panic disorder, learning disabilities, ALS, psychoses, autism, and altered behaviors, including disorders in feeding, sleep patterns, balance, and perception. In addition, elevated expression of this gene product in regions of the brain indicates that it plays a role in normal neural function. Potentially, this gene product is involved in synapse formation, neurotransmission, learning, cognition, homeostasis, or neuronal differentiation or survival. Moreover, the gene or gene product may also play a role in the treatment and/or detection of developmental disorders associated with the developing embryo, sexually-linked disorders, or disorders of the cardiovascular system. Furthermore, the protein product may also show utility in the treatment and/or prevention of a variety

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of vascular disorders, particularly embolism, aneurysm, stroke, atherosclerosis, or microvascular disease. Protein, as well as, antibodies directed against the protein may show utility as a tumor marker and/or immunotherapy targets for the above listed tissues.

Many polynucleotide sequences, such as EST sequences, are publicly available and accessible through sequence databases. Some of these sequences are related to SEQ ID NO:86 and may have been publicly available prior to conception of the present invention. Preferably, such related polynucleotides are specifically excluded from the scope of the present invention. To list every related sequence is cumbersome. Accordingly, preferably excluded from the present invention are one or more polynucleotides comprising a nucleotide sequence described by the general formula of a-b, where a is any integer between 1 to 1022 of SEQ ID NO:86, b is an integer of 15 to 1036, where both a and b correspond to the positions of nucleotide residues shown in SEQ ID NO:86, and where b is greater than or equal to a + 14.

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FEATURES OF PROTEIN ENCODED BY GENE NO: 77

In specific embodiments, polypeptides of the invention comprise, or alternatively consist of, the following amino acid sequences: TNGIMQYVTFCVWLILFSIMFLRFIQAVACISTSFLFLAEYYSIIWIYHNSFTYSS FVSAVWLL (SEQ ID NO:779), YNFMFNFSKNCQKVFHSGCIIYIPTGNVQGFLF FHILALTNT SFXXXFCFFIIATLVDVKWHLIVLICISLMTNDIILFLCAYGSK VFPWRNVPSSPLPFQNLVICLLLFSF KKFWPGAVAHL (SEQ ID NO:780), CVTQARVQWRDLGSLQPPPPGFKRFSCLSLLSRXDYMHLPPRPANFCIFSKM GFHHVGQAGLEVLXSSDL PALASQSAXITGEPLRLARIS (SEQ ID NO:781), LILFSIMFLRFIQAVACISTSFLF (SEQ ID NO:783), and/or LPPRPANFCIFSK MGFHHVGQAGLE (SEQ ID NO:782). Moreover, fragments and variants of these polypeptides (such as, for example, fragments as described herein, polypeptides at least 80%, 85%, 90%, 95%, 96%, 97%, 98%, or 99% identical to these polypeptides and polypeptides encoded by the polynucleotide which hybridizes, under stringent

conditions, to the polynucleotide encoding these polypeptides) are encompassed by the invention. Antibodies that bind polypeptides of the invention are also encompassed by the invention. Polynucleotides encoding these polypeptides are also encompassed by the invention.

This gene is expressed primarily in kidney medulla.

Polynucleotides and polypeptides of the invention are useful as reagents for differential identification of the tissue(s) or cell type(s) present in a biological sample and for diagnosis of diseases and conditions which include, but are not limited to, metabolic and renal disorders. Similarly, polypeptides and antibodies directed to these polypeptides are useful in providing immunological probes for differential identification of the tissue(s) or cell type(s). For a number of disorders of the above tissues or cells, particularly of the metabolic and renal systems, expression of this gene at significantly higher or lower levels may be routinely detected in certain tissues or cell types (e.g., renal, urogenital, endocrine, and cancerous and wounded tissues) or bodily fluids (e.g., lymph, serum, plasma, urine, synovial fluid and spinal fluid) or another tissue or cell sample taken from an individual having such a disorder, relative to the standard gene expression level, i.e., the expression level in healthy tissue or bodily fluid from an individual not having the disorder.

The tissue distribution in kidney tissue indicates that the protein products of this gene are useful for study, treatment and diagnosis of metabolic and renal diseases and disorders. Moreover, this gene or gene product could be used in the treatment and/or detection renal failure, nephritus, renal tubular acidosis, proteinuria, pyuria, edema, pyelonephritis, hydronephritis, nephrotic syndrome, crush syndrome, glomerulonephritis, hematuria, renal colic and kidney stones, in addition to Wilms Tumor Disease, and congenital kidney abnormalities such as horseshoe kidney, polycystic kidney, and Falconi's syndrome. Protein, as well as, antibodies directed against the protein may show utility as a tumor marker and/or immunotherapy targets for the above listed tissues.

Many polynucleotide sequences, such as EST sequences, are publicly available and accessible through sequence databases. Some of these sequences are related to SEQ ID NO:87 and may have been publicly available prior to conception of the present invention. Preferably, such related polynucleotides are specifically

excluded from the scope of the present invention. To list every related sequence is cumbersome. Accordingly, preferably excluded from the present invention are one or more polynucleotides comprising a nucleotide sequence described by the general formula of a-b, where a is any integer between 1 to 894 of SEQ ID NO:87, b is an integer of 15 to 908, where both a and b correspond to the positions of nucleotide residues shown in SEQ ID NO:87, and where b is greater than or equal to a + 14.

FEATURES OF PROTEIN ENCODED BY GENE NO: 78

In specific embodiments, polypeptides of the invention comprise, or alternatively consist of, the following amino acid sequences: ALVPSPQQILPSCFSLMWQVTTKSALVFFKCIYIPFLSAPSLPRLENCLIFCSLD VQSQLVFLSSPPVAGVLFFFLLSPLGSKSCSTVEX (SEQ ID NO:784), and/or APSLPRLENCLIFCSLDVQSQLVFLS (SEQ ID NO:785). Moreover, fragments and variants of these polypeptides (such as, for example, fragments as described herein, polypeptides at least 80%, 85%, 90%, 95%, 96%, 97%, 98%, or 99% identical to these polypeptides and polypeptides encoded by the polynucleotide which hybridizes, under stringent conditions, to the polynucleotide encoding these polypeptides) are encompassed by the invention. Antibodies that bind polypeptides of the invention are also encompassed by the invention. Polynucleotides encoding these polypeptides are also encompassed by the invention.

This gene is expressed in chronic synovitis and microvascular endothelium.

Polynucleotides and polypeptides of the invention are useful as reagents for differential identification of the tissue(s) or cell type(s) present in a biological sample and for diagnosis of diseases and conditions which include, but are not limited to, skeletal or vascular disorders, such as arthritis and atherosclerosis. Similarly, polypeptides and antibodies directed to these polypeptides are useful in providing immunological probes for differential identification of the tissue(s) or cell type(s). For a number of disorders of the above tissues or cells, particularly of the vascular and skeletal systems, expression of this gene at significantly higher or lower levels may be routinely detected in certain tissues or cell types (e.g., skeletal, synovium,

endothelial cells, vascular, and cancerous and wounded tissues) or bodily fluids (e.g., lymph, serum, plasma, urine, synovial fluid and spinal fluid) or another tissue or cell sample taken from an individual having such a disorder, relative to the standard gene expression level, i.e., the expression level in healthy tissue or bodily fluid from an individual not having the disorder.

The tissue distribution in synovium and microvascular endothelium indicates that the protein products of this gene are useful for study, diagnosis and treatment of arthritic and other inflammatory diseases as well as cardiovascular diseases. Moreover, the expression of this gene product in synovium would suggest a role in the detection and treatment of disorders and conditions affecting the skeletal system, in particular osteoporosis, bone cancer, as well as, disorders afflicting connective tissues (e.g. arthritis, trauma, tendonitis, chrondomalacia and inflammation), such as in the diagnosis or treatment of various autoimmune disorders such as rheumatoid arthritis, lupus, scleroderma, and dermatomyositis as well as dwarfism, spinal deformation, and specific joint abnormalities as well as chondrodysplasias (i.e. spondyloepiphyseal dysplasia congenita, familial osteoarthritis, Atelosteogenesis type II, metaphyseal chondrodysplasia type Schmid). In addition, the protein would also be useful in the treatment and/or prevention of a variety of vascular disorders, which include, but are not limited to, microvascular disease, embolism, thrombosis, aneurysm, stroke, or atherosclerosis. Protein, as well as, antibodies directed against the protein may show utility as a tumor marker and/or immunotherapy targets for the above listed tissues.

Many polynucleotide sequences, such as EST sequences, are publicly available and accessible through sequence databases. Some of these sequences are related to SEQ ID NO:88 and may have been publicly available prior to conception of the present invention. Preferably, such related polynucleotides are specifically excluded from the scope of the present invention. To list every related sequence is cumbersome. Accordingly, preferably excluded from the present invention are one or more polynucleotides comprising a nucleotide sequence described by the general formula of a-b, where a is any integer between 1 to 641 of SEQ ID NO:88, b is an integer of 15 to 655, where both a and b correspond to the positions of nucleotide residues shown in SEQ ID NO:88, and where b is greater than or equal to a + 14.

FEATURES OF PROTEIN ENCODED BY GENE NO: 79

In specific embodiments, polypeptides of the invention comprise, or alternatively consist of, the following amino acid sequences: SSPSRVRLRHTPG (SEQ ID NO:786), and/or SNTNYCFMFFYFPVKVLVPFKNCYILSLLILPCCICGHQFPRXQACTFCLHTLG GFSFSXLFLVLLSFYVQTGFSV (SEQ ID NO:787). Moreover, fragments and variants of these polypeptides (such as, for example, fragments as described herein, polypeptides at least 80%, 85%, 90%, 95%, 96%, 97%, 98%, or 99% identical to these polypeptides and polypeptides encoded by the polynucleotide which hybridizes, under stringent conditions, to the polynucleotide encoding these polypeptides) are encompassed by the invention. Antibodies that bind polypeptides of the invention are also encompassed by the invention. Polynucleotides encoding these polypeptides are also encompassed by the invention.

This gene is expressed in resting T-cells and activated monocytes.

Polynucleotides and polypeptides of the invention are useful as reagents for differential identification of the tissue(s) or cell type(s) present in a biological sample and for diagnosis of diseases and conditions which include, but are not limited to, immune or hematopoietic disorders. Similarly, polypeptides and antibodies directed to these polypeptides are useful in providing immunological probes for differential identification of the tissue(s) or cell type(s). For a number of disorders of the above tissues or cells, particularly of the immune system, expression of this gene at significantly higher or lower levels may be routinely detected in certain tissues or cell types (e.g., immune, hematopoietic, and cancerous and wounded tissues) or bodily fluids (e.g., lymph, serum, plasma, urine, synovial fluid and spinal fluid) or another tissue or cell sample taken from an individual having such a disorder, relative to the standard gene expression level, i.e., the expression level in healthy tissue or bodily fluid from an individual not having the disorder.

The tissue distribution in T-cells and monocytes indicates that the protein products of this gene are useful for the study and treatment of immune diseases such

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as inflammatory conditions. This gene product may be involved in the regulation of cytokine production, antigen presentation, or other processes that may also suggest a usefulness in the treatment of cancer (e.g. by boosting immune responses). Since the gene is expressed in cells of lymphoid origin, the natural gene product may be involved in immune functions. Therefore it may be also used as an agent for immunological disorders including arthritis, asthma, immunodeficiency diseases such as AIDS, leukemia, rheumatoid arthritis, granulomatous disease, inflammatory bowel disease, sepsis, acne, neutropenia, neutrophilia, psoriasis, hypersensitivities, such as T-cell mediated cytotoxicity; immune reactions to transplanted organs and tissues, such as host-versus-graft and graft-versus-host diseases, or autoimmunity disorders, such as autoimmune infertility, lens tissue injury, demyelination, systemic lupus erythematosis, drug induced hemolytic anemia, rheumatoid arthritis, Sjogren's disease, scleroderma and tissues. In addition, this gene product may have commercial utility in the expansion of stem cells and committed progenitors of various blood lineages, and in the differentiation and/or proliferation of various cell types. Protein, as well as, antibodies directed against the protein may show utility as a tumor marker and/or immunotherapy targets for the above listed tissues.

Many polynucleotide sequences, such as EST sequences, are publicly available and accessible through sequence databases. Some of these sequences are related to SEQ ID NO:89 and may have been publicly available prior to conception of the present invention. Preferably, such related polynucleotides are specifically excluded from the scope of the present invention. To list every related sequence is cumbersome. Accordingly, preferably excluded from the present invention are one or more polynucleotides comprising a nucleotide sequence described by the general formula of a-b, where a is any integer between 1 to 1088 of SEQ ID NO:89, b is an integer of 15 to 1102, where both a and b correspond to the positions of nucleotide residues shown in SEQ ID NO:89, and where b is greater than or equal to a + 14.

FEATURES OF PROTEIN ENCODED BY GENE NO: 80

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In specific embodiments, polypeptides of the invention comprise, or alternatively consist of, the following amino acid sequences: GTSRHGQRPIAPGTPWQREPRVEVMDPAGGPRGVLPRPCRXLVLLNPRGGKG KALQLFRSHVQPLLAEAEISFTLMLTERRNHARELVRSEELGRWXALVVMXG D GLMHEVVNGLHGAA (SEQ ID NO:788), and/or RPIAPGTPWQREPRVEVMDPAGGP (SEQ ID NO:789). Moreover, fragments and variants of these polypeptides (such as, for example, fragments as described herein, polypeptides at least 80%, 85%, 90%, 95%, 96%, 97%, 98%, or 99% identical to these polypeptides and polypeptides encoded by the polynucleotide which hybridizes, under stringent conditions, to the polynucleotide encoding these polypeptides) are encompassed by the invention. Antibodies that bind polypeptides of the invention are also encompassed by the invention. Polynucleotides encoding these polypeptides are also encompassed by the invention.

The gene encoding the disclosed cDNA is believed to reside on chromosome 17. Accordingly, polynucleotides related to this invention are useful as a marker in linkage analysis for chromosome 17.

This gene is expressed in a variety of immune system tissues, e.g., neutrophils, T-cells, and TNF induced epithelial and endothelial cells.

Polynucleotides and polypeptides of the invention are useful as reagents for differential identification of the tissue(s) or cell type(s) present in a biological sample and for diagnosis of diseases and conditions which include, but are not limited to, infectious and immune or hematopoietic disorders. Similarly, polypeptides and antibodies directed to these polypeptides are useful in providing immunological probes for differential identification of the tissue(s) or cell type(s). For a number of disorders of the above tissues or cells, particularly of the immune and vascular systems, expression of this gene at significantly higher or lower levels may be routinely detected in certain tissues or cell types (e.g., immune, hematopoietic, and cancerous and wounded tissues) or bodily fluids (e.g., lymph, serum, plasma, urine, synovial fluid and spinal fluid) or another tissue or cell sample taken from an individual having such a disorder, relative to the standard gene expression level, i.e., the expression level in healthy tissue or bodily fluid from an individual not having the disorder.

Predicted epitopes include those comprising a sequence shown in SEQ ID NO: 328 as residues: Met-1 to Trp-6.

The tissue distribution in immune tissues and cells indicates that the protein products of this gene are useful for the study and treatment of infectious diseases, immune and vascular disorders. Moreover, this gene product may be involved in the regulation of cytokine production, antigen presentation, or other processes that may also suggest a usefulness in the treatment of cancer (e.g. by boosting immune responses). Since the gene is expressed in cells of lymphoid origin, the natural gene product may be involved in immune functions. Therefore it may be also used as an agent for immunological disorders including arthritis, asthma, immunodeficiency diseases such as AIDS, leukemia, rheumatoid arthritis, granulomatous disease, inflammatory bowel disease, sepsis, acne, neutropenia, neutrophilia, psoriasis, hypersensitivities, such as T-cell mediated cytotoxicity; immune reactions to transplanted organs and tissues, such as host-versus-graft and graft-versus-host diseases, or autoimmunity disorders, such as autoimmune infertility, lens tissue injury, demyelination, systemic lupus erythematosis, drug induced hemolytic anemia, rheumatoid arthritis, Sjogren's disease, scleroderma and tissues. In addition, this gene product may have commercial utility in the expansion of stem cells and committed progenitors of various blood lineages, and in the differentiation and/or proliferation of various cell types. Protein, as well as, antibodies directed against the protein may show utility as a tumor marker and/or immunotherapy targets for the above listed tissues.

Many polynucleotide sequences, such as EST sequences, are publicly available and accessible through sequence databases. Some of these sequences are related to SEQ ID NO:90 and may have been publicly available prior to conception of the present invention. Preferably, such related polynucleotides are specifically excluded from the scope of the present invention. To list every related sequence is cumbersome. Accordingly, preferably excluded from the present invention are one or more polynucleotides comprising a nucleotide sequence described by the general formula of a-b, where a is any integer between 1 to 1519 of SEQ ID NO:90, b is an integer of 15 to 1533, where both a and b correspond to the positions of nucleotide residues shown in SEQ ID NO:90, and where b is greater than or equal to a + 14.

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FEATURES OF PROTEIN ENCODED BY GENE NO: 81

In specific embodiments, polypeptides of the invention comprise, or alternatively consists of, the following amino acid sequence: ASGPLMGXAVLKIFE (SEQ ID NO:790). Polynucleotides encoding these polypeptides are also encompassed by the invention.

This gene is expressed in activated neutrophils.

Polynucleotides and polypeptides of the invention are useful as reagents for differential identification of the tissue(s) or cell type(s) present in a biological sample and for diagnosis of diseases and conditions which include, but are not limited to, inflammation and other immune or hematopoietic conditions. Similarly, polypeptides and antibodies directed to these polypeptides are useful in providing immunological probes for differential identification of the tissue(s) or cell type(s). For a number of disorders of the above tissues or cells, particularly of the immune system, expression of this gene at significantly higher or lower levels may be routinely detected in certain tissues or cell types (e.g., immune, hematopoietic, and cancerous and wounded tissues) or bodily fluids (e.g., lymph, serum, plasma, urine, synovial fluid and spinal fluid) or another tissue or cell sample taken from an individual having such a disorder, relative to the standard gene expression level, i.e., the expression level in healthy tissue or bodily fluid from an individual not having the disorder.

The tissue distribution in neutrophils indicates that the protein products of this gene are useful for the study and treatment of immune disorders. Moreover, this gene product may be involved in the regulation of cytokine production, antigen presentation, or other processes that may also suggest a usefulness in the treatment of cancer (e.g. by boosting immune responses). Since the gene is expressed in cells of lymphoid origin, the natural gene product may be involved in immune functions. Therefore it may be also used as an agent for immunological disorders including arthritis, asthma, immunodeficiency diseases such as AIDS, leukemia, rheumatoid arthritis, granulomatous disease, inflammatory bowel disease, sepsis, acne, neutropenia, neutrophilia, psoriasis, hypersensitivities, such as T-cell mediated

cytotoxicity; immune reactions to transplanted organs and tissues, such as host-versus-graft and graft-versus-host diseases, or autoimmunity disorders, such as autoimmune infertility, lens tissue injury, demyelination, systemic lupus erythematosis, drug induced hemolytic anemia, rheumatoid arthritis, Sjogren's disease, scleroderma and tissues. In addition, this gene product may have commercial utility in the expansion of stem cells and committed progenitors of various blood lineages, and in the differentiation and/or proliferation of various cell types. Protein, as well as, antibodies directed against the protein may show utility as a tumor marker and/or immunotherapy targets for the above listed tissues.

Many polynucleotide sequences, such as EST sequences, are publicly available and accessible through sequence databases. Some of these sequences are related to SEQ ID NO:91 and may have been publicly available prior to conception of the present invention. Preferably, such related polynucleotides are specifically excluded from the scope of the present invention. To list every related sequence is cumbersome. Accordingly, preferably excluded from the present invention are one or more polynucleotides comprising a nucleotide sequence described by the general formula of a-b, where a is any integer between 1 to 561 of SEQ ID NO:91, b is an integer of 15 to 575, where both a and b correspond to the positions of nucleotide residues shown in SEQ ID NO:91, and where b is greater than or equal to a + 14.

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FEATURES OF PROTEIN ENCODED BY GENE NO: 82

In specific embodiments, polypeptides of the invention comprise, or alternatively consist of, the following amino acid sequences: LLRSALXSPHLPTPVPLV (SEQ ID NO:791), QXRNLAQEAFKWIPQDRPTVRSRXRMGLSIRLPILASNCCALPFXXPTSPLQC LWSCHCSFQANTGLAS (SEQ ID NO:792), QMTQEPPTSVRAHGIAAWGNGCRDKNTKRLIQYWPESCSGMTKGTGVGRW GEXRAERSS (SEQ ID NO:793), and/or HGIAAWGNGCRDKNTKRLIQY (SEQ ID NO:794). Moreover, fragments and variants of these polypeptides (such as, for example, fragments as described herein, polypeptides at least 80%, 85%, 90%, 95%,

96%, 97%, 98%, or 99% identical to these polypeptides and polypeptides encoded by the polynucleotide which hybridizes, under stringent conditions, to the polynucleotide encoding these polypeptides) are encompassed by the invention. Antibodies that bind polypeptides of the invention are also encompassed by the invention. Polynucleotides encoding these polypeptides are also encompassed by the invention.

This gene is expressed in neutrophils.

Polynucleotides and polypeptides of the invention are useful as reagents for differential identification of the tissue(s) or cell type(s) present in a biological sample and for diagnosis of diseases and conditions which include, but are not limited to, inflammatory and other immune or hematopoietic conditions. Similarly, polypeptides and antibodies directed to these polypeptides are useful in providing immunological probes for differential identification of the tissue(s) or cell type(s). For a number of disorders of the above tissues or cells, particularly of the immune system, expression of this gene at significantly higher or lower levels may be routinely detected in certain tissues or cell types (e.g., immune, hematopoietic, and cancerous and wounded tissues) or bodily fluids (e.g., lymph, serum, plasma, urine, synovial fluid and spinal fluid) or another tissue or cell sample taken from an individual having such a disorder, relative to the standard gene expression level, i.e., the expression level in healthy tissue or bodily fluid from an individual not having the disorder.

Predicted epitopes include those comprising a sequence shown in SEQ ID NO: 330 as residues: Ala-83 to Thr-91.

The tissue distribution in neutrophils indicates that the protein products of this gene are useful for the study and treatment of immune disorders. Moreover, the expression of this gene product in neutrophils indicates a role in the regulation of the proliferation; survival; differentiation; and/or activation of hematopoietic cell lineages, including blood stem cells. This gene product may be involved in the regulation of cytokine production, antigen presentation, or other processes that may also suggest a usefulness in the treatment of cancer (e.g. by boosting immune responses). Since the gene is expressed in cells of lymphoid origin, the natural gene product may be involved in immune functions. Therefore it may be also used as an agent for immunological disorders including arthritis, asthma, immunodeficiency diseases such as AIDS, leukemia, rheumatoid arthritis, granulomatous disease,

inflammatory bowel disease, sepsis, acne, neutropenia, neutrophilia, psoriasis, hypersensitivities, such as T-cell mediated cytotoxicity; immune reactions to transplanted organs and tissues, such as host-versus-graft and graft-versus-host diseases, or autoimmunity disorders, such as autoimmune infertility, lens tissue injury, demyelination, systemic lupus erythematosis, drug induced hemolytic anemia, rheumatoid arthritis, Sjogren's disease, scleroderma and tissues. In addition, this gene product may have commercial utility in the expansion of stem cells and committed progenitors of various blood lineages, and in the differentiation and/or proliferation of various cell types. Protein, as well as, antibodies directed against the protein may show utility as a tumor marker and/or immunotherapy targets for the above listed tissues.

Many polynucleotide sequences, such as EST sequences, are publicly available and accessible through sequence databases. Some of these sequences are related to SEQ ID NO:92 and may have been publicly available prior to conception of the present invention. Preferably, such related polynucleotides are specifically excluded from the scope of the present invention. To list every related sequence is cumbersome. Accordingly, preferably excluded from the present invention are one or more polynucleotides comprising a nucleotide sequence described by the general formula of a-b, where a is any integer between 1 to 625 of SEQ ID NO:92, b is an integer of 15 to 639, where both a and b correspond to the positions of nucleotide residues shown in SEQ ID NO:92, and where b is greater than or equal to a + 14.

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FEATURES OF PROTEIN ENCODED BY GENE NO: 83

In specific embodiments, polypeptides of the invention comprise, or alternatively consist of, the following amino acid sequences: CERSGYTRMAMDT (SEQ ID NO:795), TGSILAVGKKYSLGSYSRGDWHMRVVGLRGLGASTLQGLLIGIKPNKPQGRG KLQGRSSRKDTVLWPSPEHPHMVSMAILVYPDLSHYSNPHSTPAALLGCWPP FREGEILGLQRPGQWPEERCDRPWLPPC (SEQ ID NO:796), GSYSRGDWHMRVVGLRGLGASTLQGLLIG (SEQ ID NO:797), and/or

STPAALLGCWPPFREGEILGLQRPGQW (SEQ ID NO:798). Moreover, fragments and variants of these polypeptides (such as, for example, fragments as described herein, polypeptides at least 80%, 85%, 90%, 95%, 96%, 97%, 98%, or 99% identical to these polypeptides and polypeptides encoded by the polynucleotide which hybridizes, under stringent conditions, to the polynucleotide encoding these polypeptides) are encompassed by the invention. Antibodies that bind polypeptides of the invention are also encompassed by the invention. Polynucleotides encoding these polypeptides are also encompassed by the invention.

This gene is expressed in human neutrophils.

Polynucleotides and polypeptides of the invention are useful as reagents for differential identification of the tissue(s) or cell type(s) present in a biological sample and for diagnosis of diseases and conditions which include, but are not limited to, inflammation and immune or hematopoietic disorders. Similarly, polypeptides and antibodies directed to these polypeptides are useful in providing immunological probes for differential identification of the tissue(s) or cell type(s). For a number of disorders of the above tissues or cells, particularly of the immune and inflammatory system, expression of this gene at significantly higher or lower levels may be routinely detected in certain tissues or cell types (e.g., immune, hematopoietic, and cancerous and wounded tissues) or bodily fluids (e.g., lymph, serum, plasma, urine, synovial fluid and spinal fluid) or another tissue or cell sample taken from an individual having such a disorder, relative to the standard gene expression level, i.e., the expression level in healthy tissue or bodily fluid from an individual not having the disorder.

The tissue distribution in neutrophils indicates that the protein products of this gene are useful for diagnosis and treatment of disorders of the inflammatory and immune systems. Moreover, expression of this gene product in neutrophils indicates a role in the regulation of the proliferation; survival; differentiation; and/or activation of hematopoietic cell lineages, including blood stem cells. This gene product may be involved in the regulation of cytokine production, antigen presentation, or other processes that may also suggest a usefulness in the treatment of cancer (e.g. by boosting immune responses). Since the gene is expressed in cells of lymphoid origin, the natural gene product may be involved in immune functions. Therefore it may be

also used as an agent for immunological disorders including arthritis, asthma, immunodeficiency diseases such as AIDS, leukemia, rheumatoid arthritis, granulomatous disease, inflammatory bowel disease, sepsis, acne, neutropenia, neutrophilia, psoriasis, hypersensitivities, such as T-cell mediated cytotoxicity; immune reactions to transplanted organs and tissues, such as host-versus-graft and graft-versus-host diseases, or autoimmunity disorders, such as autoimmune infertility, lens tissue injury, demyelination, systemic lupus erythematosis, drug induced hemolytic anemia, rheumatoid arthritis, Sjogren's disease, scleroderma and tissues. In addition, this gene product may have commercial utility in the expansion of stem cells and committed progenitors of various blood lineages, and in the differentiation and/or proliferation of various cell types. Protein, as well as, antibodies directed against the protein may show utility as a tumor marker and/or immunotherapy targets for the above listed tissues.

Many polynucleotide sequences, such as EST sequences, are publicly available and accessible through sequence databases. Some of these sequences are related to SEQ ID NO:93 and may have been publicly available prior to conception of the present invention. Preferably, such related polynucleotides are specifically excluded from the scope of the present invention. To list every related sequence is cumbersome. Accordingly, preferably excluded from the present invention are one or more polynucleotides comprising a nucleotide sequence described by the general formula of a-b, where a is any integer between 1 to 844 of SEQ ID NO:93, b is an integer of 15 to 858, where both a and b correspond to the positions of nucleotide residues shown in SEQ ID NO:93, and where b is greater than or equal to a + 14.

FEATURES OF PROTEIN ENCODED BY GENE NO: 84

In specific embodiments, polypeptides of the invention comprise, or alternatively consist of, the following amino acid sequences: TMGTWVDWLTTNTAHTPAIAAAICAEDFPQRHCGSVERSPDQAC (SEQ ID NO:799), and/or TNTAHTPAIAAAICAEDFPQRHC (SEQ ID NO:800). Moreover, fragments and variants of these polypeptides (such as, for example, fragments as

described herein, polypeptides at least 80%, 85%, 90%, 95%, 96%, 97%, 98%, or 99% identical to these polypeptides and polypeptides encoded by the polynucleotide which hybridizes, under stringent conditions, to the polynucleotide encoding these polypeptides) are encompassed by the invention. Antibodies that bind polypeptides of the invention are also encompassed by the invention. Polynucleotides encoding these polypeptides are also encompassed by the invention.

This gene is expressed in human neutrophils.

Polynucleotides and polypeptides of the invention are useful as reagents for differential identification of the tissue(s) or cell type(s) present in a biological sample and for diagnosis of diseases and conditions which include, but are not limited to, inflammatory and immune or hematopoietic disorders. Similarly, polypeptides and antibodies directed to these polypeptides are useful in providing immunological probes for differential identification of the tissue(s) or cell type(s). For a number of disorders of the above tissues or cells, particularly of the inflammatory and immune systems, expression of this gene at significantly higher or lower levels may be routinely detected in certain tissues or cell types (e.g., immune, hematopoietic, and cancerous and wounded tissues) or bodily fluids (e.g., lymph, serum, plasma, urine, synovial fluid and spinal fluid) or another tissue or cell sample taken from an individual having such a disorder, relative to the standard gene expression level, i.e., the expression level in healthy tissue or bodily fluid from an individual not having the disorder.

The tissue distribution in neutrophils indicates that the protein products of this gene are useful for diagnosis and treatment of disorders of the immune and inflammatory systems. Moreover, the expression of this gene product indicates a role in the regulation of the proliferation; survival; differentiation; and/or activation of hematopoietic cell lineages, including blood stem cells. This gene product may be involved in the regulation of cytokine production, antigen presentation, or other processes that may also suggest a usefulness in the treatment of cancer (e.g. by boosting immune responses). Since the gene is expressed in cells of lymphoid origin, the natural gene product may be involved in immune functions. Therefore it may be also used as an agent for immunological disorders including arthritis, asthma, immunodeficiency diseases such as AIDS, leukemia, rheumatoid arthritis,

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granulomatous disease, inflammatory bowel disease, sepsis, acne, neutropenia, neutrophilia, psoriasis, hypersensitivities, such as T-cell mediated cytotoxicity; immune reactions to transplanted organs and tissues, such as host-versus-graft and graft-versus-host diseases, or autoimmunity disorders, such as autoimmune infertility, lens tissue injury, demyelination, systemic lupus erythematosis, drug induced hemolytic anemia, rheumatoid arthritis, Sjogren's disease, scleroderma and tissues. In addition, this gene product may have commercial utility in the expansion of stem cells and committed progenitors of various blood lineages, and in the differentiation and/or proliferation of various cell types. Protein, as well as, antibodies directed against the protein may show utility as a tumor marker and/or immunotherapy targets for the above listed tissues.

Many polynucleotide sequences, such as EST sequences, are publicly available and accessible through sequence databases. Some of these sequences are related to SEQ ID NO:94 and may have been publicly available prior to conception of the present invention. Preferably, such related polynucleotides are specifically excluded from the scope of the present invention. To list every related sequence is cumbersome. Accordingly, preferably excluded from the present invention are one or more polynucleotides comprising a nucleotide sequence described by the general formula of a-b, where a is any integer between 1 to 512 of SEQ ID NO:94, b is an integer of 15 to 526, where both a and b correspond to the positions of nucleotide residues shown in SEQ ID NO:94, and where b is greater than or equal to a + 14.

P0004-2/E350 Docket No.

FEATURES OF PROTEIN ENCODED BY GENE NO: 85

In specific embodiments, polypeptides of the invention comprise, or alternatively consist of, the following amino acid sequences: MSPETKGKGRSFPLK (SEQ ID NO:801), CQNKCSETTCGRTRRESNKQARAMAFIFKGKDLPFPFVSGDIQPKSSGSMAPD QQGLCYLGSWRSHLYCRLLPMDQVSPALC (SEQ ID NO:802), KPSPGLAYCSLSWSFHMLFLNICSGITIPVILSSGPSHLSTLSLAVSPRRPGTWV KACSCWCP (SEQ ID NO:803), NKQARAMAFIFKGKDLPFPFVSGDI (SEQ ID

NO:804), YLGSWRSHLYCRLLPMDQVSP (SEQ ID NO:805), and/or GITIPVILSSGPSHLSTLSLAVSPR (SEQ ID NO:806). Moreover, fragments and variants of these polypeptides (such as, for example, fragments as described herein, polypeptides at least 80%, 85%, 90%, 95%, 96%, 97%, 98%, or 99% identical to these polypeptides and polypeptides encoded by the polynucleotide which hybridizes, under stringent conditions, to the polynucleotide encoding these polypeptides) are encompassed by the invention. Antibodies that bind polypeptides of the invention are also encompassed by the invention. Polynucleotides encoding these polypeptides are also encompassed by the invention.

This gene is expressed in activated neutrophils.

Polynucleotides and polypeptides of the invention are useful as reagents for differential identification of the tissue(s) or cell type(s) present in a biological sample and for diagnosis of diseases and conditions which include, but are not limited to, inflammation and immune or hematopoietic diseases. Similarly, polypeptides and antibodies directed to these polypeptides are useful in providing immunological probes for differential identification of the tissue(s) or cell type(s). For a number of disorders of the above tissues or cells, particularly of the immune system and inflammatory system, expression of this gene at significantly higher or lower levels may be routinely detected in certain tissues or cell types (e.g., immune, hematopoietic, and cancerous and wounded tissues) or bodily fluids (e.g., lymph, serum, plasma, urine, synovial fluid and spinal fluid) or another tissue or cell sample taken from an individual having such a disorder, relative to the standard gene expression level, i.e., the expression level in healthy tissue or bodily fluid from an individual not having the disorder.

The tissue distribution in neutrophils indicates that the protein products of this gene are useful for diagnosis and treatment of diseases of the inflammatory and immune systems. Moreover, the expression of this gene product indicates a role in the regulation of the proliferation; survival; differentiation; and/or activation of hematopoietic cell lineages, including blood stem cells. This gene product may be involved in the regulation of cytokine production, antigen presentation, or other processes that may also suggest a usefulness in the treatment of cancer (e.g. by boosting immune responses). Since the gene is expressed in cells of lymphoid origin,

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the natural gene product may be involved in immune functions. Therefore it may be also used as an agent for immunological disorders including arthritis, asthma, immunodeficiency diseases such as AIDS, leukemia, rheumatoid arthritis, granulomatous disease, inflammatory bowel disease, sepsis, acne, neutropenia, neutrophilia, psoriasis, hypersensitivities, such as T-cell mediated cytotoxicity; immune reactions to transplanted organs and tissues, such as host-versus-graft and graft-versus-host diseases, or autoimmunity disorders, such as autoimmune infertility, lens tissue injury, demyelination, systemic lupus erythematosis, drug induced hemolytic anemia, rheumatoid arthritis, Sjogren's disease, scleroderma and tissues. In addition, this gene product may have commercial utility in the expansion of stem cells and committed progenitors of various blood lineages, and in the differentiation and/or proliferation of various cell types. Protein, as well as, antibodies directed against the protein may show utility as a tumor marker and/or immunotherapy targets for the above listed tissues.

Many polynucleotide sequences, such as EST sequences, are publicly available and accessible through sequence databases. Some of these sequences are related to SEQ ID NO:95 and may have been publicly available prior to conception of the present invention. Preferably, such related polynucleotides are specifically excluded from the scope of the present invention. To list every related sequence is cumbersome. Accordingly, preferably excluded from the present invention are one or more polynucleotides comprising a nucleotide sequence described by the general formula of a-b, where a is any integer between 1 to 412 of SEQ ID NO:95, b is an integer of 15 to 426, where both a and b correspond to the positions of nucleotide residues shown in SEQ ID NO:95, and where b is greater than or equal to a + 14.

FEATURES OF PROTEIN ENCODED BY GENE NO: 86

In specific embodiments, polypeptides of the invention comprise, or alternatively consist of, the following amino acid sequences: LERLGVGRGLE (SEQ ID NO:807),

DLPPCWTTLKEHQCFMQYQLFTIQCKVVEQTICEDERKMESTCLTLAXPESV

RQXCPATLWSSMNIC (SEQ ID NO:808), and/or TNRVXLSWRKEEQRMGRTETGAKDKGRDFLERGSRGWQLYTGAADTEEV (SEQ ID NO:809). Moreover, fragments and variants of these polypeptides (such as, for example, fragments as described herein, polypeptides at least 80%, 85%, 90%, 95%, 96%, 97%, 98%, or 99% identical to these polypeptides and polypeptides encoded by the polynucleotide which hybridizes, under stringent conditions, to the polynucleotide encoding these polypeptides) are encompassed by the invention. Antibodies that bind polypeptides of the invention are also encompassed by the invention. Polynucleotides encoding these polypeptides are also encompassed by the invention.

This gene is expressed in activated neutrophils.

Polynucleotides and polypeptides of the invention are useful as reagents for differential identification of the tissue(s) or cell type(s) present in a biological sample and for diagnosis of diseases and conditions which include, but are not limited to, inflammation and immune system disorders. Similarly, polypeptides and antibodies directed to these polypeptides are useful in providing immunological probes for differential identification of the tissue(s) or cell type(s). For a number of disorders of the above tissues or cells, particularly of the inflammatory and immune system, expression of this gene at significantly higher or lower levels may be routinely detected in certain tissues or cell types (e.g., immune, hematopoietic, and cancerous and wounded tissues) or bodily fluids (e.g., lymph, serum, plasma, urine, synovial fluid and spinal fluid) or another tissue or cell sample taken from an individual having such a disorder, relative to the standard gene expression level, i.e., the expression level in healthy tissue or bodily fluid from an individual not having the disorder.

Predicted epitopes include those comprising a sequence shown in SEQ ID NO: 334 as residues: Met-1 to Gly-6, Gly-32 to Pro-43, Leu-55 to Gln-60.

The tissue distribution in neutrophils indicates that the protein products of this gene are useful for diagnosis and treatment of disorders of the immune and inflammatory system. Moreover, the expression of this gene product indicates a role in the regulation of the proliferation; survival; differentiation; and/or activation of hematopoietic cell lineages, including blood stem cells. This gene product may be involved in the regulation of cytokine production, antigen presentation, or other

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processes that may also suggest a usefulness in the treatment of cancer (e.g. by boosting immune responses). Since the gene is expressed in cells of lymphoid origin, the natural gene product may be involved in immune functions. Therefore it may be also used as an agent for immunological disorders including arthritis, asthma, immunodeficiency diseases such as AIDS, leukemia, rheumatoid arthritis, granulomatous disease, inflammatory bowel disease, sepsis, acne, neutropenia, neutrophilia, psoriasis, hypersensitivities, such as T-cell mediated cytotoxicity; immune reactions to transplanted organs and tissues, such as host-versus-graft and graft-versus-host diseases, or autoimmunity disorders, such as autoimmune infertility, lens tissue injury, demyelination, systemic lupus erythematosis, drug induced hemolytic anemia, rheumatoid arthritis, Sjogren's disease, scleroderma and tissues. In addition, this gene product may have commercial utility in the expansion of stem cells and committed progenitors of various blood lineages, and in the differentiation and/or proliferation of various cell types. Protein, as well as, antibodies directed against the protein may show utility as a tumor marker and/or immunotherapy targets for the above listed tissues.

Many polynucleotide sequences, such as EST sequences, are publicly available and accessible through sequence databases. Some of these sequences are related to SEQ ID NO:96 and may have been publicly available prior to conception of the present invention. Preferably, such related polynucleotides are specifically excluded from the scope of the present invention. To list every related sequence is cumbersome. Accordingly, preferably excluded from the present invention are one or more polynucleotides comprising a nucleotide sequence described by the general formula of a-b, where a is any integer between 1 to 830 of SEQ ID NO:96, b is an integer of 15 to 844, where both a and b correspond to the positions of nucleotide residues shown in SEQ ID NO:96, and where b is greater than or equal to a + 14.

FEATURES OF PROTEIN ENCODED BY GENE NO: 87

In specific embodiments, polypeptides of the invention comprise, or alternatively consists of, an amino acid sequence selected from the group:

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EQVLALLWPRFELILEMNVQSVRSTDPQRLGGLDTRPHYITRRYAEFSSALVSI NQTIPNERTMQLLGQLQVEVENFVLRVAAEFSSRKEQLVFLINNYDMMLGVL MERAADDSKEVESFQQLLNARTQEFIEELLSPPFGGLVAFVKEAEALIERGQA ERLRGEEARVTQLIRGFGSSWKSSVESLSQDVMRSFTNFRNGTSIIQG (SEQ ID NO:810), ALLKYRFFYQFLLGNERATAKEIRDEYVETLSKIYLSYYRSYL GRLMKVQYEEVAEKDDLMGVEDTAKKGFXSKPSLRSRNTIFTLGTRGSVISP TELEAPILVPHTAQR (SEQ ID NO:811), EQRYPFEALFRSQHYXLLDNSCREYLFICEFFVVSGPXAHDLFHAVMGRTLS MTLKHLDSYLADCYDAIAVFLCIHIVLRFRNIAAKRDVPALDRYW (SEQ ID NO:812), GGLDTRPHYITRRYAEFSSALVSINQ (SEQ ID NO:813), SRKEQLVFLINNYDMMLGVL (SEQ ID NO:814), ALLKYRFFYQFLLGNERATAKEIRDEYVETLSKIYLSYYRSYLGRLMKVQYE EVAEKDDLMGVEDTAKKGFXSKPSLRSRNTIFTLGTRGSVISPTELEAPILVPH TAQRXEQRYPFEALFRSQHYXLLDNSCREYLFICEFFVVSGPXAHDLFHAVM GRTLSMTLKHLDSYLADCYDAIAVFLCIHIVLRFRNIAAKRDVPALDRYWEQ VLALLWPRFELILEMNVQSVRSTDPQRLGGLDTRPHYITRRYAEFSSALVSIN QTIPNERTMQLLGQLQVEVENFVLRVAAEFSSRKEQLVFLINNYDMMLGVL MERAADDSKEVESFQQLLNARTQEFIEELLSPPFGGLVAFVKEAEALIERGQA ERLRGEEARVTQLIRGFGSSWKSSVESLSQDVMRSFTNFRNGTS (SEQ ID NO:815), PADLRAVSGTSEVGLMLLELHHKVVNVDELSPGREGSELRLGQHPVEAMIEL DQLGQRSLNDTGAISEVGETPHYILTQRFH (SEQ ID NO:816), and/or GPHPGASHSAAXEQRYPFEALFRSQHYXLLDNSCREYLFICEFFVVSGPXAHD LFHAVMGRTLSMTLKHLDSYLADCYDAIAVFLCIHIVLRFRNIAAKRDVPAL DRYWGTGACLAMATV (SEQ ID NO:817). Moreover, fragments and variants of these polypeptides (such as, for example, fragments as described herein, polypeptides at least 80%, 85%, 90%, 95%, 96%, 97%, 98%, or 99% identical to these polypeptides and polypeptides encoded by the polynucleotide which hybridizes, under stringent conditions, to the polynucleotide encoding these polypeptides) are encompassed by the invention. Antibodies that bind polypeptides of the invention are also encompassed by the invention. Polynucleotides encoding these polypeptides are also encompassed by the invention.

FORM PCT/GB/99/03903

The translation product of this gene shares sequence homology with a suppressor of actin mutation which is thought to be important in mutation suppression.

This gene is expressed primarily in fetal liver.

Polynucleotides and polypeptides of the invention are useful as reagents for differential identification of the tissue(s) or cell type(s) present in a biological sample and for diagnosis of diseases and conditions which include, but are not limited to, hepatic or metabolic conditions. Similarly, polypeptides and antibodies directed to these polypeptides are useful in providing immunological probes for differential identification of the tissue(s) or cell type(s). For a number of disorders of the above tissues or cells, particularly of the liver or cancer, expression of this gene at significantly higher or lower levels may be routinely detected in certain tissues or cell types (e.g., hepatic, metabolic, and cancerous and wounded tissues) or bodily fluids (e.g., lymph, bile, serum, plasma, urine, synovial fluid and spinal fluid) or another tissue or cell sample taken from an individual having such a disorder, relative to the standard gene expression level, i.e., the expression level in healthy tissue or bodily fluid from an individual not having the disorder.

Predicted epitopes include those comprising a sequence shown in SEQ ID NO: 335 as residues: Val-53 to Arg-60, Thr-88 to Thr-94, Ala-142 to Ser-150, Gly-188 to Glu-196, Gly-208 to Ser-214, Thr-227 to Gly-232, Lys-279 to Phe-285.

The tissue distribution in liver, combined with the homology to a highly conserved suppressor of actin mutation, suggest that the protein product of this gene is useful for diagnosis and treatment of liver disorders or cancer. Similarly, the protein product of this gene is useful for the detection and treatment of hepatoblastoma, jaundice, hepatitis, liver metabolic diseases and conditions that are attributable to the differentiation of hepatocyte progenitor cells. In addition the expression in fetus would suggest a useful role for the protein product in developmental abnormalities, fetal deficiencies, pre-natal disorders and various would-healing models and/or tissue trauma. Protein, as well as, antibodies directed against the protein may show utility as a tumor marker and/or immunotherapy targets for the above listed tissues.

Many polynucleotide sequences, such as EST sequences, are publicly available and accessible through sequence databases. Some of these sequences are related to SEQ ID NO:97 and may have been publicly available prior to conception of the present invention. Preferably, such related polynucleotides are specifically excluded from the scope of the present invention. To list every related sequence is cumbersome. Accordingly, preferably excluded from the present invention are one or more polynucleotides comprising a nucleotide sequence described by the general formula of a-b, where a is any integer between 1 to 1971 of SEQ ID NO:97, b is an integer of 15 to 1985, where both a and b correspond to the positions of nucleotide residues shown in SEQ ID NO:97, and where b is greater than or equal to a + 14.

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FEATURES OF PROTEIN ENCODED BY GENE NO: 88

In specific embodiments, polypeptides of the invention comprise, or alternatively consists of, an amino acid sequence selected from the group:
YEGKEFDYVFSIDVNEGGPSYKLPYNTSDDPWLTAYNFLQKNDLNPMFLDQ
VAKFIIDNTKGQMLGLGNPSFSDPFTGGGRYVPGSSGSSNTLPTADPFTGAGR
YVPGSASMGTTMAGVDPFTGNSAYRSAASKTMNIYFPKKEAVTFDQANPTQI
LGKLKELNGTAPEEKKLTEDDLILLEKILSLICNSSSEKPTVQQLQILWKAINCP
EDIVFPALDILRLSIKHPSVNENFCNEKEGAQFSSHLINLLNPKGKPANQLLAL
RTFCNCFVGQAGQKLMMSQRESLMSHAIELKSGSNKNI (SEQ ID NO:818),
HIALATL ALNYSVCFHKD (SEQ ID NO:819),
HNIEGKAQCLSLISTILEVVQDLEATFRLLVALGTLISDDSNAVQLAKS (SEQ ID NO:820), LGVDSQIKKYSSVSEPAKVSECCRFILNLL (SEQ ID NO:821),
YEGKEFDYVFSIDVNEGGPSYKLPYNTSDDPWLTAYNFLQKNDLNPMFLDQ
VAKFIIDNTKGQMLGLGNPSFSDPFTGGGRYVPGSSGSSNTLPTADPFTGAGR
YVPGSASMGTTMAGVDPFTGNSAYRSAASKTMNIYFPKKEAVTFDQANPTQI
LGKLKELNGTAPEEKKLTEDDLILLEKILSLICNSSSEKPTVQQLQILWKAINCP
EDIVFPALDILRLSIKHPSVNENFCNEKEGAQFSSHLINLLNPKGKPANQLLAL
RTFCNCFVGQAGQKLMMSQRESLMSHAIELKSGSNKNIHIALATLALNYSVC
FHKDHNIEGKAQCLSLISTILEVVQDLEATFRLLVALGTLISDDSNAVQLAKSL

GVDSQIKKYSSVSEPAKVSECCRFILNLL(SEQ ID NO:822),
LNLLLITQKVKCWDLGIPAFQIHLQVVVG (SEQ ID NO:823),
IKHPSVNENFCNEKEGAQFSSHLINLLNP (SEQ ID NO:824),
AIELKSGSNKNIHIALATLALN (SEQ ID NO:825),
VQLAKSLGVDSQIKKYSSVSEPA (SEQ ID NO:826),
YEGKEFDYVFSIDVNEGGPSYKLPYN (SEQ ID NO:827),
AYNFLQKNDLNPMFLDQVAK FIIDNT (SEQ ID NO:828),
SFSDPFTGGGRYVPG (SEQ ID NO:829), TADPFTGAGRY (SEQ ID NO:830),
TTMAGVDPFTGNSAYRSAA (SEQ ID NO:831), NIYFPKKEA (SEQ ID NO:832),
TFDQANPTQILGKLKELNG (SEQ ID NO:833),
PEDIVFPALDILRLSIKHPSVNENFCNEKE (SEQ ID NO:834),
QFSSHLINLLNPKG KPANQLLALRTFCNCFV (SEQ ID NO:835), and/or
QAGQKLMMSQRESLMSHAIELKSGSN (SEQ ID NO:836). Moreover, fragments and variants of these polypeptides (such as, for example, fragments as described herein, polypeptides at least 80%, 85%, 90%, 95%, 96%, 97%, 98%, or 99% identical to these polypeptides and polypeptides encoded by the polynucleotide which hybridizes, under stringent conditions, to the polynucleotide encoding these polypeptides) are encompassed by the invention. Antibodies that bind polypeptides of the invention are also encompassed by the invention. Polynucleotides encoding these polypeptides are also encompassed by the invention.

These polypeptides share significant homology with phospholipase A2 activating protein, which is thought to be important in signal transduction (see, e.g., Wang et al., Gene 161(2):237-241 (1995)). The gene encoding the disclosed cDNA is believed to reside on chromosome 9. Accordingly, polynucleotides related to this invention are useful as a marker in linkage analysis for chromosome 9.

This gene is expressed primarily in endothelial cells, to a less extent in placenta, endometrial stromal cells, osteosarcoma, testis tumor, muscle, and infant brain that are likely to be rich in blood vessels.

Polynucleotides and polypeptides of the invention are useful as reagents for differential identification of the tissue(s) or cell type(s) present in a biological sample and for diagnosis of diseases and conditions which include, but are not limited to, disorders of the vascular system, aberrant angiogenesis, tumor angiogenesis, or

related disorders of endothelial tissues. Similarly, polypeptides and antibodies directed to these polypeptides are useful in providing immunological probes for differential identification of the tissue(s) or cell type(s). For a number of disorders of the above tissues or cells, particularly of the vascular system or tumors, expression of this gene at significantly higher or lower levels may be routinely detected in certain tissues or cell types (e.g., endothelial, placenta, skeletal, neural, and cancerous and wounded tissues) or bodily fluids (e.g., lymph, amniotic fluid, serum, plasma, urine, synovial fluid and spinal fluid) or another tissue or cell sample taken from an individual having such a disorder, relative to the standard gene expression level, i.e., the expression level in healthy tissue or bodily fluid from an individual not having the disorder.

The tissue distribution of this gene in endothelial cells and several potential highly vascularized tissues, combined with the homology to the highly conserved phospholipase A2 activating protein suggest that this gene may be involved in transducing signals for endothelial cells in angiogenesis or vasculogenesis. Furthermore, the protein may show utility for the treatment, and/or prevention of embolism, thrombosis, aneurysm, atherosclerosis, microvascular disease, or stroke. Protein, as well as, antibodies directed against the protein may show utility as a tumor marker and/or immunotherapy targets for the above listed tissues.

Many polynucleotide sequences, such as EST sequences, are publicly available and accessible through sequence databases. Some of these sequences are related to SEQ ID NO:98 and may have been publicly available prior to conception of the present invention. Preferably, such related polynucleotides are specifically excluded from the scope of the present invention. To list every related sequence is cumbersome. Accordingly, preferably excluded from the present invention are one or more polynucleotides comprising a nucleotide sequence described by the general formula of a-b, where a is any integer between 1 to 1402 of SEQ ID NO:98, b is an integer of 15 to 1416, where both a and b correspond to the positions of nucleotide residues shown in SEQ ID NO:98, and where b is greater than or equal to a + 14.

FEATURES OF PROTEIN ENCODED BY GENE NO: 89

In specific embodiments, polypeptides of the invention comprise, or alternatively consists of, an amino acid sequence selected from the group: YPNQDGDILRDQVLHEHIQRLSKVVTANHRALQIPEVYLREAPWPSAQSEIRT ISAYKTPRDKVQCILRMCSTIMNLLSLANEDSVPGADDFVPVLVFVLIKANPP CLLSTVQYISSFYASCLSGEESYWWMQFTAAVE (SEQ ID NO:837), YPNQDGDILRDQVLHEHIQRLSKVVTANHRALQIPEVYLREAPWPSAQSEIRT ISAYKTPRDKVQCILRMCSTIMNLLSLANEDSVPGADDFVPVLVFVLIKANPP CLLSTVQYISSFYASCLSGEESYWWMQFTAAVEFIKTI (SEQ ID NO:838), YPNQDGDILRDQVL (SEQ ID NO:839), EAPWPSAQSEI (SEQ ID NO:840), PVLVFVLIKANP (SEQ ID NO:845), SGEESYWWMQFTAAVEFIKTI (SEQ ID NO:841), ADDFVPVLVFVLIK ANPP (SEQ ID NO:842), YKTPRDKVQCIL (SEQ ID NO:843), and/or GADDFVPV LVFVLIK (SEQ ID NO:844). Moreover, fragments and variants of these polypeptides (such as, for example, fragments as described herein, polypeptides at least 80%, 85%, 90%, 95%, 96%, 97%, 98%, or 99% identical to these polypeptides and polypeptides encoded by the polynucleotide which hybridizes, under stringent conditions, to the polynucleotide encoding these polypeptides) are encompassed by the invention. Antibodies that bind polypeptides of the invention are also encompassed by the invention. Polynucleotides encoding these polypeptides are also encompassed by the invention.

The translation product of this gene shares sequence homology with human Ras inhibitor and yeast VPS9p which is thought to be important in Golgi vacuole transport. The gene encoding the disclosed cDNA is believed to reside on chromosome 9. Accordingly, polynucleotides related to this invention are useful as a marker in linkage analysis for chromosome 9.

This gene is expressed primarily in T cells and melanocytes.

Polynucleotides and polypeptides of the invention are useful as reagents for differential identification of the tissue(s) or cell type(s) present in a biological sample and for diagnosis of diseases and conditions which include, but are not limited to, immune, hematopoietic, or integumentary disorders, such as dysfunctions and disorders involving T cells and melanocytes. Similarly, polypeptides and antibodies directed to these polypeptides are useful in providing immunological probes for

differential identification of the tissue(s) or cell type(s). For a number of disorders of the above tissues or cells, particularly of the immune system, expression of this gene at significantly higher or lower levels may be routinely detected in certain tissues or cell types (e.g., cancerous and wounded tissues) or bodily fluids (e.g., lymph, serum, plasma, urine, synovial fluid and spinal fluid) or another tissue or cell sample taken from an individual having such a disorder, relative to the standard gene expression level, i.e., the expression level in healthy tissue or bodily fluid from an individual not having the disorder.

The tissue distribution in T-cells and melanocytes, combined with the homology to a Ras inhibitor, indicates that the protein product of this gene is useful for regulating signal transduction; the diagnosis and treatment of disorders involving T cells and melanocytes, and potentially in the prevention or study of immune responses to aberrant integumentary cells and tissues, particularly in tumors and cancers, such as skin cancers. Moreover, the protein product of this gene is useful for the treatment, diagnosis, and/or prevention of various skin disorders including congenital disorders (i.e. nevi, moles, freckles, Mongolian spots, hemangiomas, port-wine syndrome), integumentary tumors (i.e. keratoses, Bowen's disease, basal cell carcinoma, squamous cell carcinoma, malignant melanoma, Paget's disease, mycosis fungoides, and Kaposi's sarcoma), injuries and inflammation of the skin (i.e. wounds, rashes, prickly heat disorder, psoriasis, dermatitis), atherosclerosis, uticaria, eczema, photosensitivity, autoimmune disorders (i.e. lupus erythematosus, vitiligo, dermatomyositis, morphea, scleroderma, pemphigoid, and pemphigus), keloids, striae, erythema, petechiae, purpura, and xanthelasma. In addition, such disorders may predispose increased susceptibility to viral and bacterial infections of the skin (i.e. cold sores, warts, chickenpox, molluscum contagiosum, herpes zoster, boils, cellulitis, erysipelas, impetigo, tinea, Athlete's foot, and ringworm). Moreover, the protein product of this gene may also be useful for the treatment or diagnosis of various connective tissue disorders such as arthritis, trauma, tendonitis, chrondomalacia and inflammation, autoimmune disorders such as rheumatoid arthritis, lupus, scleroderma, and dermatomyositis as well as dwarfism, spinal deformation, and specific joint abnormalities as well as chondrodysplasias (i.e. spondyloepiphyseal dysplasia congenita, familial osteoarthritis, Atelosteogenesis type II, metaphyseal

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chondrodysplasia type Schmid). Protein, as well as, antibodies directed against the protein may show utility as a tumor marker and/or immunotherapy targets for the above listed tissues.

Many polynucleotide sequences, such as EST sequences, are publicly available and accessible through sequence databases. Some of these sequences are related to SEQ ID NO:99 and may have been publicly available prior to conception of the present invention. Preferably, such related polynucleotides are specifically excluded from the scope of the present invention. To list every related sequence is cumbersome. Accordingly, preferably excluded from the present invention are one or more polynucleotides comprising a nucleotide sequence described by the general formula of a-b, where a is any integer between 1 to 1746 of SEQ ID NO:99, b is an integer of 15 to 1760, where both a and b correspond to the positions of nucleotide residues shown in SEQ ID NO:99, and where b is greater than or equal to a + 14.

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FEATURES OF PROTEIN ENCODED BY GENE NO: 90

The translation product of this gene shares sequence homology with neuronal olfactomedin-related ER localized protein which is thought to be important in the maintenance, growth, or differentiation of chemosensory cilia on the apical dendrites of olfactory neurons. Moreover, the protein also shares homology with the conserved human AMY protein which is thought to be a glial cell-specific transforming protein.

In specific embodiments, polypeptides of the invention comprise, or alternatively consists of, an amino acid sequence selected from the group: SARASTQPPAGQHPGPC (SEQ ID NO:846), MPGRWRWQRDMHPARKLLSLLFLILMGTELTQD (SEQ ID NO:847), SAAPDSLLRSSKGSTRGSL (SEQ ID NO:848), AAIVIWRGKSESRIAKTPGI (SEQ ID NO:849), FRGGGTLVLPPTHTPEWLIL (SEQ ID NO:852), PLGITLPLGAPETGGGD (SEQ ID NO:850), NSARAS TQPPAGQHPGPCMPGRWRWQRD (SEQ ID NO:853), YIVQGTTSPFEMPTIPTPARHRAPHSPPAGHVATAPQALHIKPAMHTAGRHAG CPSRSQ RHNPHRLFLEPPRAALCPKGG (SEQ ID NO:854),

ASNAHSWPARWLPFQVSAAQSPPPVSGAPKGSVMPKGRMSHSGVCVGGRTK VPPPLKMPGVLAIRLSLFPLQMTIAAKDPLVLPFELLSRESGAAES (SEQ ID NO:855), GRMSHSGVCVGGRTKVPPPLKMPGVLA (SEQ ID NO:856), and/or CAAETWKGSQRAGQLCALLA (SEQ ID NO:851). Moreover, fragments and variants of these polypeptides (such as, for example, fragments as described herein, polypeptides at least 80%, 85%, 90%, 95%, 96%, 97%, 98%, or 99% identical to these polypeptides and polypeptides encoded by the polynucleotide which hybridizes, under stringent conditions, to the polynucleotide encoding these polypeptides) are encompassed by the invention. Antibodies that bind polypeptides of the invention are also encompassed by the invention. Polynucleotides encoding these polypeptides are also encompassed by the invention.

The gene encoding the disclosed cDNA is believed to reside on chromosome 9. Accordingly, polynucleotides related to this invention are useful as a marker in linkage analysis for chromosome 9.

This gene is expressed in pineal gland.

Polynucleotides and polypeptides of the invention are useful as reagents for differential identification of the tissue(s) or cell type(s) present in a biological sample and for diagnosis of diseases and conditions which include, but are not limited to, neurological and endocrine disorders. Similarly, polypeptides and antibodies directed to these polypeptides are useful in providing immunological probes for differential identification of the tissue(s) or cell type(s). For a number of disorders of the above tissues or cells, particularly of the neurological or endocrine systems, expression of this gene at significantly higher or lower levels may be routinely detected in certain tissues or cell types (e.g., neural, endocrine, and cancerous and wounded tissues) or bodily fluids (e.g., lymph, serum, plasma, urine, synovial fluid and spinal fluid) or another tissue or cell sample taken from an individual having such a disorder, relative to the standard gene expression level, i.e., the expression level in healthy tissue or bodily fluid from an individual not having the disorder.

Predicted epitopes include those comprising a sequence shown in SEQ ID NO: 338 as residues: Leu-20 to Ala-26, Arg-32 to Arg-39, Thr-104 to Gly-112.

The tissue distribution in pineal gland, combined with the homology to both the olfactomedin-related, and AMY proteins, indicates that the protein product of this

gene is useful for maintenance, growth, or differentiation of neuron cells in pineal gland. Therefore, the protein product of this gene may be useful for the diagnosis and treatment of neurological disorders in pineal gland. Moreover, the protein product of this gene is useful for the detection/treatment of neurodegenerative disease states, behavioral disorders, or inflammatory conditions such as Alzheimer's Disease, Parkinson's Disease, Huntington's Disease, Tourette's Syndrome, meningitis, encephalitis, demyelinating diseases, peripheral neuropathies, neoplasia, trauma, congenital malformations, spinal cord injuries, ischemia and infarction, aneurysms, hemorrhages, schizophrenia, mania, dementia, paranoia, obsessive compulsive disorder, panic disorder, learning disabilities, ALS, psychoses, autism, and altered behaviors, including disorders in feeding, sleep patterns, balance, and perception. In addition, elevated expression of this gene product in regions of the brain indicates that it plays a role in normal neural function. Potentially, this gene product is involved in synapse formation, neurotransmission, learning, cognition, homeostasis, or neuronal differentiation or survival. Moreover, the gene or gene product may also play a role in the treatment and/or detection of developmental disorders associated with the developing embryo, sexually-linked disorders, or disorders of the cardiovascular system. Protein, as well as, antibodies directed against the protein may show utility as a tumor marker and/or immunotherapy targets for the above listed tissues.

Many polynucleotide sequences, such as EST sequences, are publicly available and accessible through sequence databases. Some of these sequences are related to SEQ ID NO:100 and may have been publicly available prior to conception of the present invention. Preferably, such related polynucleotides are specifically excluded from the scope of the present invention. To list every related sequence is cumbersome. Accordingly, preferably excluded from the present invention are one or more polynucleotides comprising a nucleotide sequence described by the general formula of a-b, where a is any integer between 1 to 585 of SEQ ID NO:100, b is an integer of 15 to 599, where both a and b correspond to the positions of nucleotide residues shown in SEQ ID NO:100, and where b is greater than or equal to a + 14.

FEATURES OF PROTEIN ENCODED BY GENE NO: 91

This gene is expressed primarily in prostate and apoptotic T cells.

Polynucleotides and polypeptides of the invention are useful as reagents for differential identification of the tissue(s) or cell type(s) present in a biological sample and for diagnosis of diseases and conditions which include, but are not limited to, reproductive, immune, or hematopoietic disorders, particularly prostate disease and T cell dysfunction. Similarly, polypeptides and antibodies directed to these polypeptides are useful in providing immunological probes for differential identification of the tissue(s) or cell type(s). For a number of disorders of the above tissues or cells, particularly of the prostate cancer, expression of this gene at significantly higher or lower levels may be routinely detected in certain tissues or cell types (e.g. prostate, immune, cancerous and wounded tissues) or bodily fluids (e.g., lymph, seminal fluid, serum, plasma, urine, synovial fluid and spinal fluid) or another tissue or cell sample taken from an individual having such a disorder, relative to the standard gene expression level, i.e., the expression level in healthy tissue or bodily fluid from an individual not having the disorder.

The tissue distribution in prostate and T-cells indicates that the protein product of this gene is useful for the detection of abnormal activity in prostate and T cells, such as proliferative conditions of the prostate, or possibly treatment of this abnormality. This gene product may be involved in the regulation of cytokine production, antigen presentation, or other processes that may also suggest a usefulness in the treatment of cancer (e.g. by boosting immune responses). Since the gene is expressed in cells of lymphoid origin, the natural gene product may be involved in immune functions. Therefore it may be also used as an agent for immunological disorders including arthritis, asthma, immunodeficiency diseases such as AIDS, leukemia, rheumatoid arthritis, granulomatous disease, inflammatory bowel disease, sepsis, acne, neutropenia, neutrophilia, psoriasis, hypersensitivities, such as T-cell mediated cytotoxicity; immune reactions to transplanted organs and tissues, such as host-versus-graft and graft-versus-host diseases, or autoimmunity disorders, such as autoimmune infertility, lens tissue injury, demyelination, systemic lupus erythematosis, drug induced hemolytic anemia, rheumatoid arthritis, Sjogren's disease, scleroderma and tissues. In addition, this gene product may have commercial

utility in the expansion of stem cells and committed progenitors of various blood lineages, and in the differentiation and/or proliferation of various cell types. Protein, as well as, antibodies directed against the protein may show utility as a tumor marker and/or immunotherapy targets for the above listed tissues.

Many polynucleotide sequences, such as EST sequences, are publicly available and accessible through sequence databases. Some of these sequences are related to SEQ ID NO:101 and may have been publicly available prior to conception of the present invention. Preferably, such related polynucleotides are specifically excluded from the scope of the present invention. To list every related sequence is cumbersome. Accordingly, preferably excluded from the present invention are one or more polynucleotides comprising a nucleotide sequence described by the general formula of a-b, where a is any integer between 1 to 770 of SEQ ID NO:101, b is an integer of 15 to 784, where both a and b correspond to the positions of nucleotide residues shown in SEQ ID NO:101, and where b is greater than or equal to a + 14.

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FEATURES OF PROTEIN ENCODED BY GENE NO: 92

The gene encoding the disclosed cDNA is believed to reside on chromosome 19. Accordingly, polynucleotides related to this invention are useful as a marker in linkage analysis for chromosome 19.

This gene is expressed primarily in prostate, and to a lesser extent, in smooth muscle cells, fibroblasts, and placenta.

Polynucleotides and polypeptides of the invention are useful as reagents for differential identification of the tissue(s) or cell type(s) present in a biological sample and for diagnosis of diseases and conditions which include, but are not limited to, disorders in prostate or vascular tissues. Similarly, polypeptides and antibodies directed to these polypeptides are useful in providing immunological probes for differential identification of the tissue(s) or cell type(s). For a number of disorders of the above tissues or cells, particularly of the prostate or vascular system, expression of this gene at significantly higher or lower levels may be routinely detected in certain tissues or cell types (e.g. prostate, musculoskeletal, cancerous and wounded tissues)

or bodily fluids (e.g., lymph, seminal fluid, serum, plasma, urine, synovial fluid and spinal fluid) or another tissue or cell sample taken from an individual having such a disorder, relative to the standard gene expression level, i.e., the expression level in healthy tissue or bodily fluid from an individual not having the disorder.

Predicted epitopes include those comprising a sequence shown in SEQ ID NO: 340 as residues: Ser-38 to Lys-46.

The tissue distribution in prostate and smooth muscle indicates that the protein product of this gene is useful for regulating the function of prostate or highly vascularized tissues, such as the placenta. Similarly, the protein product of this gene may be useful in the treatment and/or detection of vascular disorders which include, but are not limited to, stroke, embolism, thrombosis, aneurysm, microvascular disease, or atherosclerosis. The protein may also show utility in the treatment or detection of proliferative disorders of the prostate or male reproductive system. Protein, as well as, antibodies directed against the protein may show utility as a tumor marker and/or immunotherapy targets for the above listed tissues.

Many polynucleotide sequences, such as EST sequences, are publicly available and accessible through sequence databases. Some of these sequences are related to SEQ ID NO:102 and may have been publicly available prior to conception of the present invention. Preferably, such related polynucleotides are specifically excluded from the scope of the present invention. To list every related sequence is cumbersome. Accordingly, preferably excluded from the present invention are one or more polynucleotides comprising a nucleotide sequence described by the general formula of a-b, where a is any integer between 1 to 390 of SEQ ID NO:102, b is an integer of 15 to 404, where both a and b correspond to the positions of nucleotide residues shown in SEQ ID NO:102, and where b is greater than or equal to a + 14.

FEATURES OF PROTEIN ENCODED BY GENE NO: 93

In specific embodiments, polypeptides of the invention comprise, or alternatively consists of, the following amino acid sequence: GHQTAPETPSRSD (SEQ ID NO:857). Moreover, fragments and variants of this polypeptide (such as, for

example, fragments as described herein, polypeptides at least 80%, 85%, 90%, 95%, 96%, 97%, 98%, or 99% identical to these polypeptides and polypeptides encoded by the polynucleotide which hybridize, under stringent conditions, to the polynucleotide encoding this polypeptide are encompassed by the invention. Antibodies that bind polypeptides of the invention are also encompassed by the invention. Polynucleotides encoding this polypeptide are also encompassed by the invention.

This gene is expressed primarily in embryos and fetal tissues, and to a lesser extent, in proliferative tissues.

Polynucleotides and polypeptides of the invention are useful as reagents for differential identification of the tissue(s) or cell type(s) present in a biological sample and for diagnosis of diseases and conditions which include, but are not limited to, disorders in embryonic development and cell proliferation. Similarly, polypeptides and antibodies directed to these polypeptides are useful in providing immunological probes for differential identification of the tissue(s) or cell type(s). For a number of disorders of the above tissues or cells, particularly of the embryonic tissues and proliferative cells, expression of this gene at significantly higher or lower levels may be routinely detected in certain tissues or cell types (e.g., developmental, differentiating, and cancerous and wounded tissues) or bodily fluids (e.g., lymph, amniotic fluid, serum, plasma, urine, synovial fluid and spinal fluid) or another tissue or cell sample taken from an individual having such a disorder, relative to the standard gene expression level, i.e., the expression level in healthy tissue or bodily fluid from an individual not having the disorder.

The tissue distribution in embryonic and fetal tissues indicates that the protein product of this gene is useful for the diagnosis or treatment of abnormalities in developing and proliferative cells and organs. Similarly, expression within embryonic tissue and other cellular sources marked by proliferating cells indicates that this protein may play a role in the regulation of cellular division, and may show utility in the diagnosis and treatment of cancer and other proliferative disorders. Similarly, developmental tissues rely on decisions involving cell differentiation and/or apoptosis in pattern formation. Thus, this protein may also be involved in apoptosis or tissue differentiation and could again be useful in cancer therapy.

Protein, as well as, antibodies directed against the protein may show utility as a tumor marker and/or immunotherapy targets for the above listed tissues.

Many polynucleotide sequences, such as EST sequences, are publicly available and accessible through sequence databases. Some of these sequences are related to SEQ ID NO:103 and may have been publicly available prior to conception of the present invention. Preferably, such related polynucleotides are specifically excluded from the scope of the present invention. To list every related sequence is cumbersome. Accordingly, preferably excluded from the present invention are one or more polynucleotides comprising a nucleotide sequence described by the general formula of a-b, where a is any integer between 1 to 2204 of SEQ ID NO:103, b is an integer of 15 to 2218, where both a and b correspond to the positions of nucleotide residues shown in SEQ ID NO:103, and where b is greater than or equal to a + 14.

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FEATURES OF PROTEIN ENCODED BY GENE NO: 94

The translation product of this gene shares sequence homology with a transformation related protein which is thought to be important in transformation.

In specific embodiments, polypeptides of the invention comprise, or alternatively consists of, the following amino acid sequence: SQTDR (SEQ ID NO:858). Polynucleotides encoding this polypeptides are also encompassed by the invention. Antibodies that bind polypeptides of the invention are also encompassed by the invention.

The gene encoding the disclosed cDNA is believed to reside on chromosome 2. Accordingly, polynucleotides related to this invention are useful as a marker in linkage analysis for chromosome 2.

This gene is expressed primarily in female reproductive tissues, i.e., breast cancer cells, placenta, and ovary, and to a lesser extent, in fetal lung.

Polynucleotides and polypeptides of the invention are useful as reagents for differential identification of the tissue(s) or cell type(s) present in a biological sample and for diagnosis of diseases and conditions which include, but are not limited to, cancer or dysfunction of reproductive tissues, in addition to pulmonary or

developmental disorders. Similarly, polypeptides and antibodies directed to these polypeptides are useful in providing immunological probes for differential identification of the tissue(s) or cell type(s). For a number of disorders of the above tissues or cells, particularly of the reproduction system, expression of this gene at significantly higher or lower levels may be routinely detected in certain tissues or cell types (e.g., pulmonary, reproductive, ovarian, breast, placental, developmental, and cancerous and wounded tissues) or bodily fluids (e.g., lymph, pulmonary surfactant or sputum, amniotic fluid, serum, plasma, urine, synovial fluid and spinal fluid) or another tissue or cell sample taken from an individual having such a disorder, relative to the standard gene expression level, i.e., the expression level in healthy tissue or bodily fluid from an individual not having the disorder.

Predicted epitopes include those comprising a sequence shown in SEQ ID NO: 342 as residues: Ser-50 to Pro-61.

The tissue distribution in female reproductive tissues, combined with the homology to the transformation related protein, indicates that the protein product of this gene is useful for the diagnosis and treatment of conditions caused by transformation, i.e. tumorigenesis in reproductive organs, (e.g. breast, placenta, and ovary). Similarly, expression within fetal tissue and other cellular sources marked by proliferating cells indicates that this protein may play a role in the regulation of cellular division, and may show utility in the diagnosis and treatment of cancer and other proliferative disorders. Similarly, developmental tissues rely on decisions involving cell differentiation and/or apoptosis in pattern formation. Thus this protein may also be involved in apoptosis or tissue differentiation and could again be useful in cancer therapy. Protein may also be useful in the treatment or detection of a variety of pulmonary conditions, including, but not limited to emphysema, ARDS, cystic fibrosis, asthma, etc. Protein, as well as, antibodies directed against the protein may show utility as a tumor marker and/or immunotherapy targets for the above listed tissues.

Many polynucleotide sequences, such as EST sequences, are publicly available and accessible through sequence databases. Some of these sequences are related to SEQ ID NO:104 and may have been publicly available prior to conception of the present invention. Preferably, such related polynucleotides are specifically

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excluded from the scope of the present invention. To list every related sequence is cumbersome. Accordingly, preferably excluded from the present invention are one or more polynucleotides comprising a nucleotide sequence described by the general formula of a-b, where a is any integer between 1 to 1337 of SEQ ID NO:104, b is an integer of 15 to 1351, where both a and b correspond to the positions of nucleotide residues shown in SEQ ID NO:104, and where b is greater than or equal to a + 14.

FEATURES OF PROTEIN ENCODED BY GENE NO: 95

In specific embodiments, polypeptides of the invention comprise, or alternatively consist of, the following amino acid sequences: NIYFKEKRKRGGAKMAGAIIEN (SEQ ID NO:859), VYLCAYTSTINVTVTTANAKLINMCCLVDSNTRSCVVIDEGIFRSAEQFLIKFR NKQSTIFPRFTWELHSIGLVFSIVFMGWCIQEHQSKDIQIPHPIDACEKGTVHL DCDAAPFPMAFRYLTNDEEDDSHGSAGQGDKHEELEPKN (SEQ ID NO:860), KMPCRMSPNSSIQVQSNPMENHSTGILIKVMEIPRAKMTFSRSTGGRDIMVILL QYHTIMMKMLGVRKVFMANHTLVKPPFWWIPTNRISFISPIPTLIFFFSFTGSR MFKR (SEQ ID NO:861), TTKSEKMQKSPWTFPWLTVMTHLLSGLKWPMKEYHGNSNAPSHLPRLQSM RAVTMNVMSFLSWKLGLWPISFTF (SEQ ID NO:862), IKFRNKQSTIFPRFTWELHSIGLVFSIVFMG (SEQ ID NO:863), SSIQVQSNPMENHSTGILIKVMEIPRAKM (SEQ ID NO:864), and/or LGVRKVFMANHTLVKPPFWWIPTNRISFISPIP (SEQ ID NO:865). Moreover, fragments and variants of these polypeptides (such as, for example, fragments as described herein, polypeptides at least 80%, 85%, 90%, 95%, 96%, 97%, 98%, or 99% identical to these polypeptides and polypeptides encoded by the polynucleotide which hybridizes, under stringent conditions, to the polynucleotide encoding these polypeptides) are encompassed by the invention. Antibodies that bind polypeptides of the invention are also encompassed by the invention. Polynucleotides encoding these polypeptides are also encompassed by the invention.

Polynucleotides encoding these polypeptides are also encompassed by the invention. The gene encoding the disclosed cDNA is believed to reside on chromosome 1. Accordingly, polynucleotides related to this invention are useful as a marker in linkage analysis for chromosome 1.

This gene is expressed primarily in testes, rhabdomyosarcoma, infant brain and to a lesser extent in some tumors and highly vascularized tissues.

Polynucleotides and polypeptides of the invention are useful as reagents for differential identification of the tissue(s) or cell type(s) present in a biological sample and for diagnosis of diseases and conditions which include, but are not limited to, tumorigenesis, abnormal angiogenesis, reproductive, vascular, and/or neurological disorders. , Similarly, polypeptides and antibodies directed to these polypeptides are useful in providing immunological probes for differential identification of the tissue(s) or cell type(s). For a number of disorders of the above tissues or cells, particularly of the tumor tissues or vascular tissues, expression of this gene at significantly higher or lower levels may be routinely detected in certain tissues or cell types (e.g., muscle, neural, developmental, vascular, reproductive, testicular, and cancerous and wounded tissues) or bodily fluids (e.g., lymph, serum, seminal fluid, amniotic fluid, plasma, urine, synovial fluid and spinal fluid) or another tissue or cell sample taken from an individual having such a disorder, relative to the standard gene expression level, i.e., the expression level in healthy tissue or bodily fluid from an individual not having the disorder.

Predicted epitopes include those comprising a sequence shown in SEQ ID NO: 343 as residues: Arg-46 to Trp-54, Pro-60 to Ile-69, Asn-116 to Ala-122, Arg-147 to Lys-153, Ser-158 to Glu-170, Ile-399 to Ser-405, Pro-486 to Met-499, Pro-502 to Asp-508.

The tissue distribution in infant brain indicates that the protein product of this gene is useful for a range of disease states including treatment of tumor or vascular disorders and the treatment of neurological disorders such as Alzheimer's Disease, Parkinson's Disease, Huntington's Disease, schizophrenia, mania, dementia, paranoia, obsessive compulsive disorder and panic disorder. Moreover, expression within vascular tissues indicates that the protein product of this gene is useful in the treatment and/or detection of a variety of vascular conditions, which include but are

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not limited to emphysema, atherosclerosis, thrombosis, microvascular disease, stroke or aneurysm. Protein, as well as, antibodies directed against the protein may show utility as a tumor marker and/or immunotherapy targets for the above listed tissues.

Many polynucleotide sequences, such as EST sequences, are publicly available and accessible through sequence databases. Some of these sequences are related to SEQ ID NO:105 and may have been publicly available prior to conception of the present invention. Preferably, such related polynucleotides are specifically excluded from the scope of the present invention. To list every related sequence is cumbersome. Accordingly, preferably excluded from the present invention are one or more polynucleotides comprising a nucleotide sequence described by the general formula of a-b, where a is any integer between 1 to 2052 of SEQ ID NO:105, b is an integer of 15 to 2066, where both a and b correspond to the positions of nucleotide residues shown in SEQ ID NO:105, and where b is greater than or equal to a + 14.

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FEATURES OF PROTEIN ENCODED BY GENE NO: 96

The translation product of this gene is homologous to the Clostridium perfringens enterotoxin (CPE) receptor gene product and shares sequence homology with a human ORF specific to prostate and a glycoprotein specific to oligodendrocytes, both of which are tissue specific proteins. See e.g., Katahira et al. J Cell Biol. 136(6):1239-1247 (1997). PMID: 9087440; UI: 97242441.

In specific embodiments, polypeptides of the invention comprise, or alternatively consist of, the following amino acid sequences: TMASMGLQV (SEQ ID NO:866),
KSWMMLWAVQDTGTITIRPANRNTTPATIMVLALALSSSRQLVHLPPTTDSST PRAATMMLMMTRARAACRSCGSASSESYTLHCIWPVLCTTQFIHRPSQMVCE VTMLLPMKAVTRHMGSAQHSMTASQPRTASAMPITCSPMEAIVQRPRELRT WKAEGIRLWGP (SEQ ID NO:867),
LQVMGIALAVLGWLAVMLCCALPMWRVT (SEQ ID NO:868),
SNIVTSQTIWEGLWMNCVVQST (SEQ ID NO:869),
QMQCKVYDSLLALPQDLQ (SEQ ID NO:870),

KCTNCLEDESAKAKTMIV(SEQ ID NO:871), GVVFLLAGLMVIVPVSWTAHNIIQDFYNPLVA (SEQ ID NO:872), and/or CCNCPPRTDKPY (SEQ ID NO:873). Moreover, fragments and variants of these polypeptides (such as, for example, fragments as described herein, polypeptides at least 80%, 85%, 90%, 95%, 96%, 97%, 98%, or 99% identical to these polypeptides and polypeptides encoded by the polynucleotide which hybridizes, under stringent conditions, to the polynucleotide encoding these polypeptides) are encompassed by the invention. Antibodies that bind polypeptides of the invention are also encompassed by the invention. Polynucleotides encoding these polypeptides are also encompassed by the invention.

The gene encoding the disclosed cDNA is believed to reside on chromosome 7. Accordingly, polynucleotides related to this invention are useful as a marker in linkage analysis for chromosome 7.

This gene is expressed primarily in pancreas tumor and ulcerative colitis, and to a lesser extent in several tumors and normal tissues.

Polynucleotides and polypeptides of the invention are useful as reagents for differential identification of the tissue(s) or cell type(s) present in a biological sample and for diagnosis of diseases and conditions which include, but are not limited to, metabolic, gastrointestinal, or proliferative disorders, such as pancreatic disorders, ulcerative colitis, tumors and food poisoning. Similarly, polypeptides and antibodies directed to these polypeptides are useful in providing immunological probes for differential identification of the tissue(s) or cell type(s). For a number of disorders of the above tissues or cells, particularly of the digestive system or tumorigenic system, expression of this gene at significantly higher or lower levels may be routinely detected in certain tissues or cell types (e.g., metabolic, gastrointestinal, pancreatic, and cancerous and wounded tissues) or bodily fluids (e.g., lymph, bile, serum, plasma, urine, synovial fluid and spinal fluid) or another tissue or cell sample taken from an individual having such a disorder, relative to the standard gene expression level, i.e., the expression level in healthy tissue or bodily fluid from an individual not having the disorder.

Predicted epitopes include those comprising a sequence shown in SEQ ID NO: 344 as residues: Gly-147 to Met-152, Cys-177 to Lys-188.

The tissue distribution in pancreas, combined with the homology to a prostate and oligodendrocyte-specific protein, indicates that the protein product of this gene is useful as a marker for the diagnosis or treatment of disorders in pancreas, ulcerative colitis, and tumors. Furthermore, identity to the human receptor for Clostridium perfringenes enterotoxin indicates that the soluble portion of this receptor could be used in the treatment of food poisoning associated with Clostridia perfringens by blocking the activity of the perfringens enterotoxin. Protein, as well as, antibodies directed against the protein may show utility as a tumor marker and/or immunotherapy targets for the above listed tissues.

Many polynucleotide sequences, such as EST sequences, are publicly available and accessible through sequence databases. Some of these sequences are related to SEQ ID NO:106 and may have been publicly available prior to conception of the present invention. Preferably, such related polynucleotides are specifically excluded from the scope of the present invention. To list every related sequence is cumbersome. Accordingly, preferably excluded from the present invention are one or more polynucleotides comprising a nucleotide sequence described by the general formula of a-b, where a is any integer between 1 to 1691 of SEQ ID NO:106, b is an integer of 15 to 1705, where both a and b correspond to the positions of nucleotide residues shown in SEQ ID NO:106, and where b is greater than or equal to a + 14.

D6W7N5.300202

FEATURES OF PROTEIN ENCODED BY GENE NO: 97

The translation product of this gene shares sequence homology with an ATPase from Saccharomyces cerevisiae which is thought to be important in metabolism (See Genbank Accession No.g1181253).

In specific embodiments, polypeptides of the invention comprise, or alternatively consist of, the following amino acid sequences: PFTAIAGSEIFSLE (SEQ ID NO:874), SKTEALTQAFR (SEQ ID NO:875), VVHTVSLHEIDVINSRTQGFLALF (SEQ ID NO:876), PGVLFIDEVHMLDIE (SEQ ID NO:877),

AGIRQRFSARLWQLVSIMATVTATTKVPEIRDVTRIERIGAHSHIRGLGLDDAL
EPRQASQGMVGQLAARRAAGVVLEMIREGKIAGRAVLIAGQPGTGKTAIAM
GMAQALGPDTPFTAIAGSEIFSLEMSKTEALTQAFRRSIGVRIKEETEIIEGEVV
EIQIDRPATGTGSKVGKLTLKTTEMETIYDLGTKMIXSLTKDKVQAGDVITID
KATGKISKLGRSFTRARELRRYGLPDQVRAVPRWGAPETQGGGAHRVPARD
RRHQLSHPGLPGALLR (SEQ ID NO:878),
SPSTRRRARSPSWAAPSHAPANYDAMGSQTKFVQCPDGELQKRKEVVHTVS
LHEIDVINSRTQGFLALFSGDTGEIKSEVREQINAKVAEWREEGKAEIIPGVLFI
DEVHMLDIESFSFLNRALESDMAPVQQVYGDAVRALVAGAPDSRDATVGGL
VPNSCSPGDPLVLERPPPRWXS (SEQ ID NO:879),
WIPRAAGIRHEATNRGITRIRGTSYQSPHGIPIDLLDRRHVTLQGPVEEGEALD
VQHVDLVDEQHSRDDLRLALLAPLSHLGIDLLTDF (SEQ ID NO:880),
YDAMGSQTKFVQCPDGELQKRKEVVHTVSL (SEQ ID NO:881),
KAEIIPGVLFIDEVHMLDIESFSFLNRALES (SEQ ID NO:882), and/or
EATNRGITRIRGTSYQSPHGIPIDLLDR (SEQ ID NO:883). Moreover, fragments and variants of these polypeptides (such as, for example, fragments as described herein, polypeptides at least 80%, 85%, 90%, 95%, 96%, 97%, 98%, or 99% identical to these polypeptides and polypeptides encoded by the polynucleotide which hybridizes, under stringent conditions, to the polynucleotide encoding these polypeptides) are encompassed by the invention. Antibodies that bind polypeptides of the invention are also encompassed by the invention. Polynucleotides encoding these polypeptides are also encompassed by the invention.

This gene is expressed primarily in testes and several hematopoietic cells.

Polynucleotides and polypeptides of the invention are useful as reagents for differential identification of the tissue(s) or cell type(s) present in a biological sample and for diagnosis of diseases and conditions which include, but are not limited to, reproductive, immune, or hematopoietic disorders, particularly male infertility and leukemia. Similarly, polypeptides and antibodies directed to these polypeptides are useful in providing immunological probes for differential identification of the tissue(s) or cell type(s). For a number of disorders of the above tissues or cells, particularly of the hematopoietic system, expression of this gene at significantly higher or lower levels may be routinely detected in certain tissues or cell types (e.g.,

reproductive, immune, hematopoietic, testicular, and cancerous and wounded tissues) or bodily fluids (e.g., lymph, seminal fluid, serum, plasma, urine, synovial fluid and spinal fluid) or another tissue or cell sample taken from an individual having such a disorder, relative to the standard gene expression level, i.e., the expression level in healthy tissue or bodily fluid from an individual not having the disorder.

The tissue distribution in testes and hematopoietic cells, combined with the homology to ATPases, indicates that the protein product of this gene is useful as a marker for the diagnosis and treatment of leukemia and other hematopoietic disorders. The protein may also show utility as a contraceptive, or for the treatment and/or detection of aberrant testicular function. The secreted protein can also be used to determine biological activity, to raise antibodies, as tissue markers, to isolate cognate ligands or receptors, to identify agents that modulate their interactions and as nutritional supplements. It may also have a very wide range of biological activities. Typical of these are cytokine, cell proliferation/differentiation modulating activity or induction of other cytokines; immunostimulating/immunosuppressant activities (e.g. for treating human immunodeficiency virus infection, cancer, autoimmune diseases and allergy); regulation of hematopoiesis (e.g. for treating anemia or as adjunct to chemotherapy); stimulation or growth of bone, cartilage, tendons, ligaments and/or nerves (e.g. for treating wounds); stimulation of follicle stimulating hormone (for control of fertility); chemotactic and chemokinetic activities (e.g. for treating infections, tumors); hemostatic or thrombolytic activity (e.g. for treating hemophilia, cardiac infarction etc.); anti-inflammatory activity (e.g. for treating septic shock, Crohn's disease); as antimicrobials; for treating psoriasis or other hyperproliferative diseases; for regulation of metabolism, and behavior. Also contemplated is the use of the corresponding nucleic acid in gene therapy procedures. Protein, as well as, antibodies directed against the protein may show utility as a tumor marker and/or immunotherapy targets for the above listed tissues.

Many polynucleotide sequences, such as EST sequences, are publicly available and accessible through sequence databases. Some of these sequences are related to SEQ ID NO:107 and may have been publicly available prior to conception of the present invention. Preferably, such related polynucleotides are specifically excluded from the scope of the present invention. To list every related sequence is

cumbersome. Accordingly, preferably excluded from the present invention are one or more polynucleotides comprising a nucleotide sequence described by the general formula of a-b, where a is any integer between 1 to 1153 of SEQ ID NO:107, b is an integer of 15 to 1167, where both a and b correspond to the positions of nucleotide residues shown in SEQ ID NO:107, and where b is greater than or equal to a + 14.

FEATURES OF PROTEIN ENCODED BY GENE NO: 98

In specific embodiments, polypeptides of the invention comprise, or alternatively consists of, an amino acid sequence selected from the group: MRSARPSLGCLPSWAFSQALNI (SEQ ID NO:884), LLGLKGLAPAEISAVCEGNFN (SEQ ID NO:885), VAHGLAWSYYIGYLRLILPELQARIR (SEQ ID NO:886),TYNQHYNNLLRGAVSQRC (SEQ ID NO:887), ILLPLDCGVPDNLS MADPNIRFLDKLPQQTGDRAGIKDRVYSN (SEQ ID NO:888), SIYELLENGQRAGTCVLEYATPLQTLFAMSQYSQAGFSGEDRLEQ (SEQ ID NO:889), AKLFCRTLEDILADAPESQNNCRLIAYQEPADDSSFSLSQEVLRHLRQEEKEE VTVGSLKTSAVPSTSTMSQEPELLISGMEKPLPLRTDFS (SEQ ID NO:890), LRLHSEKLPLAARSAGPSLLVIIQSSQCPGGRRYRGSYWRTVRACLGCPLRRG ALLLLSIYFYYSLPNAVGPPFTW (SEQ ID NO:892), VWLTPTFASWINCPSRPVTVLASRIGFTATASMSFWRTGSGRAPVSWSTPPPC RLCLPCHNTVKLALAGRIGLSRPNSSAGHLRTSWQMPLSLRTTAASLPTRNLQ MTAASRCPRRFSGTCGRRKRKRLLWAA (SEQ ID NO:893), GVCQVSFMGPSRPTPHPSPLPLPGDAELSQWYQQAPSPSGSWSCSIIGEPQQK NGEEEEAEFGVLNPPAPTLQHQGCYGLSCRATLA (SEQ ID NO:894), and/or LLGLKGLAPAEISAVCEKGNFNVAHGLAWSYYIGYLRLILPEL (SEQ ID NO:891). Moreover, fragments and variants of these polypeptides (such as, for example, fragments as described herein, polypeptides at least 80%, 85%, 90%, 95%, 96%, 97%, 98%, or 99% identical to these polypeptides and polypeptides encoded by the polynucleotide which hybridizes, under stringent conditions, to the polynucleotide

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encoding these polypeptides) are encompassed by the invention. Antibodies that bind polypeptides of the invention are also encompassed by the invention. Polynucleotides encoding these polypeptides are also encompassed by the invention.

This gene is expressed primarily in prostate BPH, and to a lesser extent, in bone marrow.

Polynucleotides and polypeptides of the invention are useful as reagents for differential identification of the tissue(s) or cell type(s) present in a biological sample and for diagnosis of diseases and conditions which include, but are not limited to, reproductive, hematopoietic, or immune disorders, particularly benign prostatic hypertrophy, prostate cancer, or leukemia. Similarly, polypeptides and antibodies directed to these polypeptides are useful in providing immunological probes for differential identification of the tissue(s) or cell type(s). For a number of disorders of the above tissues or cells, particularly of the male urinary system, expression of this gene at significantly higher or lower levels may be routinely detected in certain tissues or cell types (e.g., reproductive, hematopoietic, immune, prostatic, and cancerous and wounded tissues) or bodily fluids (e.g., lymph, seminal fluid, serum, plasma, urine, synovial fluid and spinal fluid) or another tissue or cell sample taken from an individual having such a disorder, relative to the standard gene expression level, i.e., the expression level in healthy tissue or bodily fluid from an individual not having the disorder.

Predicted epitopes include those comprising a sequence shown in SEQ ID NO: 346 as residues: Ile-60 to Asn-69, Leu-106 to Asp-112, Glu-130 to Gly-136, Phe-160 to Glu-167, Pro-184 to Cys-190, Glu-197 to Ser-202, Arg-215 to Glu-221, Thr-237 to Pro-242.

The tissue distribution in prostate tissue indicates that the protein product of this gene is useful for the diagnosis or treatment of reproductive disorders, such as benign prostatic hypertrophy or prostate cancer. Moreover, the protein product of this gene is useful for the treatment and diagnosis of hematopoetic related disorders such as anemia, pancytopenia, leukopenia, thrombocytopenia or leukemia since stromal cells are important in the production of cells of hematopoietic lineages. The uses include bone marrow cell ex vivo culture, bone marrow transplantation, bone marrow reconstitution, radiotherapy or chemotherapy of neoplasia. The gene product may

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also be involved in lymphopoiesis, therefore, it can be used in immune disorders such as infection, inflammation, allergy, immunodeficiency etc. In addition, this gene product may have commercial utility in the expansion of stem cells and committed progenitors of various blood lineages, and in the differentiation and/or proliferation of various cell types. Protein, as well as, antibodies directed against the protein may show utility as a tumor marker and/or immunotherapy targets for the above listed tissues.

Many polynucleotide sequences, such as EST sequences, are publicly available and accessible through sequence databases. Some of these sequences are related to SEQ ID NO:108 and may have been publicly available prior to conception of the present invention. Preferably, such related polynucleotides are specifically excluded from the scope of the present invention. To list every related sequence is cumbersome. Accordingly, preferably excluded from the present invention are one or more polynucleotides comprising a nucleotide sequence described by the general formula of a-b, where a is any integer between 1 to 1893 of SEQ ID NO:108, b is an integer of 15 to 1907, where both a and b correspond to the positions of nucleotide residues shown in SEQ ID NO:108, and where b is greater than or equal to a + 14.

D0E3N5N0-D0E3N5N0

FEATURES OF PROTEIN ENCODED BY GENE NO: 99

The gene encoding the disclosed cDNA is believed to reside on chromosome 15. Accordingly, polynucleotides related to this invention are useful as a marker in linkage analysis for chromosome 15.

This gene is expressed primarily in salivary gland.

Polynucleotides and polypeptides of the invention are useful as reagents for differential identification of the tissue(s) or cell type(s) present in a biological sample and for diagnosis of diseases and conditions which include, but are not limited to, metabolic disorders, particularly of the salivary gland. Similarly, polypeptides and antibodies directed to these polypeptides are useful in providing immunological probes for differential identification of the tissue(s) or cell type(s). For a number of disorders of the above tissues or cells, particularly of glandular tissues, expression of

this gene at significantly higher or lower levels may be routinely detected in certain tissues or cell types (e.g. salivary gland, cancerous and wounded tissues) or bodily fluids (e.g., lymph, serum, chyme, plasma, urine, synovial fluid and spinal fluid) or another tissue or cell sample taken from an individual having such a disorder, relative to the standard gene expression level, i.e., the expression level in healthy tissue or bodily fluid from an individual not having the disorder.

The tissue distribution in salivary glands indicates that the protein product of this gene is useful for the treatment and/or detection of disorders of or injuries to the salivary gland or other glandular tissue. Protein, as well as, antibodies directed against the protein may show utility as a tumor marker and/or immunotherapy targets for the above listed tissues.

Many polynucleotide sequences, such as EST sequences, are publicly available and accessible through sequence databases. Some of these sequences are related to SEQ ID NO:109 and may have been publicly available prior to conception of the present invention. Preferably, such related polynucleotides are specifically excluded from the scope of the present invention. To list every related sequence is cumbersome. Accordingly, preferably excluded from the present invention are one or more polynucleotides comprising a nucleotide sequence described by the general formula of a-b, where a is any integer between 1 to 597 of SEQ ID NO:109, b is an integer of 15 to 611, where both a and b correspond to the positions of nucleotide residues shown in SEQ ID NO:109, and where b is greater than or equal to a + 14.

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FEATURES OF PROTEIN ENCODED BY GENE NO: 100

The translation product of this gene shares sequence homology with a C.elegans gene. Based upon its degree of conservation, an important cellular function can be attributed to this protein. When tested against Jurkat cell lines, supernatants removed from cells containing this gene activated the GAS (gamma activating sequence) promoter element. Thus, it is likely that this gene activates T-cells through the JAK-STAT signal transduction pathway. GAS is a promoter element found upstream of many genes which are involved in the Jak-STAT pathway. The Jak-

STAT pathway is a large, signal transduction pathway involved in the differentiation and proliferation of cells. Therefore, activation of the Jak-STAT pathway, reflected by the binding of the GAS element, can be used to indicate proteins involved in the proliferation and differentiation of cells.

In specific embodiments, polypeptides of the invention comprise, or alternatively consists of, an amino acid sequence selected from the group: DPRVRLNSLTCKHIFISLTQ (SEQ ID NO:902), TMKLLKLRRNIVKLSLYRHFTN (SEQ ID NO:895), TLILAVAASIVFIIWTTMKFRI (SEQ ID NO:896), VTCQSDWRELWVDDAIWRLLFSMILFVI (SEQ ID NO:897), MVLWRPSANNQRFAFSPLSEEEEEDEQ (SEQ ID NO:898), MVLWRPSANNQRFAFSPLSEEEEEDEQ (SEQ ID NO:899), KEPMLKESFEGMKMRSTKQEPNGNSKVNKAQEDDL (SEQ ID NO:900), NAFGRHSTAVK (SEQ ID NO:903), ESCLLCGISEYPIQRXICPGCFDPCRXAFSSETLTGSNPGHHSQSGIWHRQATP GVTLHKVVVAXALYLLFSGMEGVLRVTGAQTDLASLAFIPLAFLDTALCWW IFISLTQTMKLLKLRRNIVKLSLYRHFTNTLILAVAASIVFIIWTTMKFRIVTCQ SDWRELWVDDAIWRLLFSMILFVIMVLWRPSANNQRFAFSPLSEEEEEDEQK EPMLKESFEGMKMRSTKQEPNGNSKVNKAQEDDLKWVEENVPSSVTDVALP ALLDSDEERMITHFERSKME (SEQ ID NO:904), and/or KWVEENVPSSVTDVALPALLDSDEERMITHFERSKME (SEQ ID NO:901). Moreover, fragments and variants of these polypeptides (such as, for example, fragments as described herein, polypeptides at least 80%, 85%, 90%, 95%, 96%, 97%, 98%, or 99% identical to these polypeptides and polypeptides encoded by the polynucleotide which hybridizes, under stringent conditions, to the polynucleotide encoding these polypeptides) are encompassed by the invention. Antibodies that bind polypeptides of the invention are also encompassed by the invention. Polynucleotides encoding these polypeptides are also encompassed by the invention.

The gene encoding the disclosed cDNA is believed to reside on chromosome 15. Accordingly, polynucleotides related to this invention are useful as a marker in linkage analysis for chromosome 15.

This gene is expressed primarily in thyroid, and to a lesser extent, in osteoclastoma, kidney medulla, and lung.

Polynucleotides and polypeptides of the invention are useful as reagents for differential identification of the tissue(s) or cell type(s) present in a biological sample and for diagnosis of diseases and conditions which include, but are not limited to, endocrine disorders, particularly thyroid dysfunction or cancer. Similarly, polypeptides and antibodies directed to these polypeptides are useful in providing immunological probes for differential identification of the tissue(s) or cell type(s). For a number of disorders of the above tissues or cells, particularly of the endocrine system, expression of this gene at significantly higher or lower levels may be routinely detected in certain tissues or cell types (e.g., endocrine, skeletal, urogenital, renal, pulmonary, and cancerous and wounded tissues) or bodily fluids (e.g., lymph, pulmonary surfactant or sputum, serum, plasma, urine, synovial fluid and spinal fluid) or another tissue or cell sample taken from an individual having such a disorder, relative to the standard gene expression level, i.e., the expression level in healthy tissue or bodily fluid from an individual not having the disorder.

Predicted epitopes include those comprising a sequence shown in SEQ ID NO: 348 as residues: Lys-107 to Leu-124, Glu-150 to Thr-159, Pro-173 to Asp-179, Ser-192 to Ser-201.

The tissue distribution in thyroid, combined with the detected GAS biological activity, indicates that the protein product of this gene is useful for the diagnosis and treatment of thyroid dysfunction or cancer. Protein, as well as, antibodies directed against the protein may show utility as a tumor marker and/or immunotherapy targets for the above listed tissues.

Many polynucleotide sequences, such as EST sequences, are publicly available and accessible through sequence databases. Some of these sequences are related to SEQ ID NO:110 and may have been publicly available prior to conception of the present invention. Preferably, such related polynucleotides are specifically excluded from the scope of the present invention. To list every related sequence is cumbersome. Accordingly, preferably excluded from the present invention are one or more polynucleotides comprising a nucleotide sequence described by the general formula of a-b, where a is any integer between 1 to 2618 of SEQ ID NO:110, b is an

integer of 15 to 2632, where both a and b correspond to the positions of nucleotide residues shown in SEQ ID NO:110, and where b is greater than or equal to a + 14.

FEATURES OF PROTEIN ENCODED BY GENE NO: 101

The gene encoding the disclosed cDNA is thought to reside on chromosome 16. Accordingly, polynucleotides related to this invention are useful as a marker in linkage analysis for chromosome 16.

In specific embodiments, polypeptides of the invention comprise, or alternatively consists of, an amino acid sequence selected from the group: YEPMDFXMALIYD (SEQ ID NO:905), IRHELTVLRDT RPACA (SEQ ID NO:906), and/or MDFXMALIYD (SEQ ID NO:907). Moreover, fragments and variants of these polypeptides (such as, for example, fragments as described herein, polypeptides at least 80%, 85%, 90%, 95%, 96%, 97%, 98%, or 99% identical to these polypeptides and polypeptides encoded by the polynucleotide which hybridizes, under stringent conditions, to the polynucleotide encoding these polypeptides) are encompassed by the invention. Antibodies that bind polypeptides of the invention are also encompassed by the invention. Polynucleotides encoding these polypeptides are also encompassed by the invention.

This gene is expressed primarily in kidney cortex, and to a lesser extent, in adult brain, corpus colosum, hippocampus, and frontal cortex.

Polynucleotides and polypeptides of the invention are useful as reagents for differential identification of the tissue(s) or cell type(s) present in a biological sample and for diagnosis of diseases and conditions which include, but are not limited to, neurological disorders, kidney disorders. Similarly, polypeptides and antibodies directed to these polypeptides are useful in providing immunological probes for differential identification of the tissue(s) or cell type(s). For a number of disorders of the above tissues or cells, particularly of the central nervous system and renal system, expression of this gene at significantly higher or lower levels may be routinely detected in certain tissues or cell types (e.g. kidney, brain, cancerous and wounded tissues) or bodily fluids (e.g., lymph, serum, plasma, urine, synovial fluid and spinal

fluid) or another tissue or cell sample taken from an individual having such a disorder, relative to the standard gene expression level, i.e., the expression level in healthy tissue or bodily fluid from an individual not having the disorder.

The tissue distribution in adult brain, corpus colosum, hippocampus, and frontal cortex indicates that the protein product of this gene is useful for treatment or diagnosis of neurological disorders, such as Alzheimer's Disease, Parkinson's Disease, Huntington's Disease, Tourette's Syndrome, schizophrenia, mania, dementia, paranoia, obsessive compulsive disorder, panic disorder, learning disabilities, ALS, psychoses, autism, and altered behaviors, including disorders in feeding, sleep patterns, balance, and perception. In addition, the gene or gene product may also play a role in the treatment and/or detection of developmental disorders associated with the developing embryo, or sexually-linked disorders. Furthermore, The tissue distribution in kidney indicates that this gene or gene product could be used in the treatment and/or detection of kidney diseases including renal failure, nephritus, renal tubular acidosis, proteinuria, pyuria, edema, pyelonephritis, hydronephritis, nephrotic syndrome, crush syndrome, glomerulonephritis, hematuria, renal colic and kidney stones, in addition to Wilms Tumor Disease, and congenital kidney abnormalities such as horseshoe kidney, polycystic kidney, and Falconi's syndrome. Protein, as well as, antibodies directed against the protein may show utility as a tumor marker and/or immunotherapy targets for the above listed tissues.

Many polynucleotide sequences, such as EST sequences, are publicly available and accessible through sequence databases. Some of these sequences are related to SEQ ID NO:111 and may have been publicly available prior to conception of the present invention. Preferably, such related polynucleotides are specifically excluded from the scope of the present invention. To list every related sequence is cumbersome. Accordingly, preferably excluded from the present invention are one or more polynucleotides comprising a nucleotide sequence described by the general formula of a-b, where a is any integer between 1 to 2235 of SEQ ID NO:111, b is an integer of 15 to 2249, where both a and b correspond to the positions of nucleotide residues shown in SEQ ID NO:111, and where b is greater than or equal to a + 14.

FEATURES OF PROTEIN ENCODED BY GENE NO: 102

The translation product of this gene shares sequence homology with F15C11.2 of C. elegans which is of unknown function.

In specific embodiments, polypeptides of the invention comprise, or alternatively consists of, an amino acid sequence selected from the group: MQEMMRNQDRALSNLESIPGGYNA (SEQ ID NO:908), LRRMYTDIQEPMLSAAQEQFGGNPF (SEQ ID NO:909), ASLVSNTSSGEGSQPSRTENRDPLPNPWAPQT (SEQ ID NO:910), SQSSSASSGTASTVGGTTGSTASGTSGQSTTAPNLVPGVGASMFNTPGMQSLL QQITENPQLMQNMLSAPY (SEQ ID NO:911), MRSMMQSLSQNPDLAAQMMLNNPLFAGNPQLQEQMRQQLPTFLQQ (SEQ ID NO:912), MQNPDTLSAMSNPRAMQALLQIQQGLQTLATEAPGLIPGFTPGLGALGSTGG SSGTNGSNATPSENTSPTAGT (SEQ ID NO:913), TEPGHQQFIQQMLQALAGVNPQLQNPEVRFQQQLEQLSAMGFLNREANLQA LIATGGDINAAIERLLGSQPS (SEQ ID NO:914), RNPAMMQEMMRNQDRALSNLESIPGGYNALRRMYTDIQEPMLSAA (SEQ ID NO:915), GNPFASLVSNTSS (SEQ ID NO:916), ENRDPLPNPWA (SEQ ID NO:917), GKILKDQDTLSQHGIHD (SEQ ID NO:918), GLTVHLVIKTQNRP (SEQ ID NO:919), SELQSQMQRQLLSNPEMM (SEQ ID NO:920), PEISHMLNNPDIMR (SEQ ID NO:921), and/or RQLIMANPQMQQLIQRNP (SEQ ID NO:922). Moreover, fragments and variants of these polypeptides (such as, for example, fragments as described herein, polypeptides at least 80%, 85%, 90%, 95%, 96%, 97%, 98%, or 99% identical to these polypeptides and polypeptides encoded by the polynucleotide which hybridizes, under stringent conditions, to the polynucleotide encoding these polypeptides) are encompassed by the invention. Antibodies that bind polypeptides of the invention are also encompassed by the invention. Polynucleotides encoding these polypeptides are also encompassed by the invention.

This gene is expressed primarily in breast.

Polynucleotides and polypeptides of the invention are useful as reagents for differential identification of the tissue(s) or cell type(s) present in a biological sample

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and for diagnosis of diseases and conditions which include, but are not limited to, breast cancer. Similarly, polypeptides and antibodies directed to these polypeptides are useful in providing immunological probes for differential identification of the tissue(s) or cell type(s). For a number of disorders of the above tissues or cells, particularly of tumor systems, expression of this gene at significantly higher or lower levels may be routinely detected in certain tissues or cell types (e.g. breast, cancerous and wounded tissues) or bodily fluids (e.g., lymph, serum, plasma, urine, synovial fluid and spinal fluid) or another tissue or cell sample taken from an individual having such a disorder, relative to the standard gene expression level, i.e., the expression level in healthy tissue or bodily fluid from an individual not having the disorder.

The tissue distribution in breast indicates that the protein product of this gene is useful for treatment and diagnosis of some types of breast cancer. Protein, as well as, antibodies directed against the protein may show utility as a tissue-specific marker and/or immunotherapy target for the above listed tissues.

Many polynucleotide sequences, such as EST sequences, are publicly available and accessible through sequence databases. Some of these sequences are related to SEQ ID NO:112 and may have been publicly available prior to conception of the present invention. Preferably, such related polynucleotides are specifically excluded from the scope of the present invention. To list every related sequence is cumbersome. Accordingly, preferably excluded from the present invention are one or more polynucleotides comprising a nucleotide sequence described by the general formula of a-b, where a is any integer between 1 to 2184 of SEQ ID NO:112, b is an integer of 15 to 2198, where both a and b correspond to the positions of nucleotide residues shown in SEQ ID NO:112, and where b is greater than or equal to a + 14.

FEATURES OF PROTEIN ENCODED BY GENE NO: 103

The translation product of this gene shares sequence homology with secreted serine proteases and lysozyme C precursor, which is thought to be important in bacteriolytic function.

In specific embodiments, polypeptides of the invention comprise, or alternatively consists of, an amino acid sequence selected from the group: NLCHVDCQDLLNPNLLAGIHCAKRIVS (SEQ ID NO:923), LDGFEGYSLSDWLCLAFVESKFN (SEQ ID NO:924), NENADGSFDYGLFQINSHYWCN (SEQ ID NO:925), NLCHVDCQDLLNPNLLAGIHCAKRIVS (SEQ ID NO:926), and/or EPSALSCTSSPPR (SEQ ID NO:927). Moreover, fragments and variants of these polypeptides (such as, for example, fragments as described herein, polypeptides at least 80%, 85%, 90%, 95%, 96%, 97%, 98%, or 99% identical to these polypeptides and polypeptides encoded by the polynucleotide which hybridizes, under stringent conditions, to the polynucleotide encoding these polypeptides) are encompassed by the invention. Antibodies that bind polypeptides of the invention are also encompassed by the invention. Polynucleotides encoding these polypeptides are also encompassed by the invention.

This gene is expressed primarily in testes.

Polynucleotides and polypeptides of the invention are useful as reagents for differential identification of the tissue(s) or cell type(s) present in a biological sample and for diagnosis of diseases and conditions which include, but are not limited to, infection, immune system disorders, reproductive disorders. Similarly, polypeptides and antibodies directed to these polypeptides are useful in providing immunological probes for differential identification of the tissue(s) or cell type(s). For a number of disorders of the above tissues or cells, particularly of the immune system and reproductive system, expression of this gene at significantly higher or lower levels may be routinely detected in certain tissues or cell types (e.g. testes, cancerous and wounded tissues) or bodily fluids (e.g., lymph, serum, seminal fluid, plasma, urine, synovial fluid and spinal fluid) or another tissue or cell sample taken from an individual having such a disorder, relative to the standard gene expression level, i.e., the expression level in healthy tissue or bodily fluid from an individual not having the disorder.

Predicted epitopes include those comprising a sequence shown in SEQ ID NO: 351 as residues: Ile-62 to Phe-70, Asn-78 to Asn-84.

The tissue distribution in testes, combined with the homology to lysozyme C precursor indicates that the protein product of this gene is useful for boosting the monocyte-macrophage system, and for enhancing the activity of immune agents. Alternatively, the tissue distribution indicates that the protein product of this gene is useful for the treatment and diagnosis of conditions concerning proper testicular function (e.g. endocrine function, sperm maturation), as well as cancer. Therefore, this gene product is useful in the treatment of male infertility and/or impotence. This gene product is also useful in assays designed to identify binding agents, as such agents (antagonists) are useful as male contraceptive agents. Similarly, the protein is believed to be useful in the treatment and/or diagnosis of testicular cancer. The testes are also a site of active gene expression of transcripts that may be expressed, particularly at low levels, in other tissues of the body. Therefore, this gene product may be expressed in other specific tissues or organs where it may play related functional roles in other processes, such as hematopoiesis, inflammation, bone formation, and kidney function, to name a few possible target indications.

Many polynucleotide sequences, such as EST sequences, are publicly available and accessible through sequence databases. Some of these sequences are related to SEQ ID NO:113 and may have been publicly available prior to conception of the present invention. Preferably, such related polynucleotides are specifically excluded from the scope of the present invention. To list every related sequence is cumbersome. Accordingly, preferably excluded from the present invention are one or more polynucleotides comprising a nucleotide sequence described by the general formula of a-b, where a is any integer between 1 to 1029 of SEQ ID NO:113, b is an integer of 15 to 1043, where both a and b correspond to the positions of nucleotide residues shown in SEQ ID NO:113, and where b is greater than or equal to a + 14.

FEATURES OF PROTEIN ENCODED BY GENE NO: 104

This gene is expressed primarily in apoptotic T-cell, and to a lesser extent in CD34(+) cells..

Polynucleotides and polypeptides of the invention are useful as reagents for differential identification of the tissue(s) or cell type(s) present in a biological sample and for diagnosis of diseases and conditions which include, but are not limited to, immune disorders. Similarly, polypeptides and antibodies directed to these polypeptides are useful in providing immunological probes for differential identification of the tissue(s) or cell type(s). For a number of disorders of the above tissues or cells, particularly of the immune system, expression of this gene at significantly higher or lower levels may be routinely detected in certain tissues or cell types (e.g. immune, cancerous and wounded tissues) or bodily fluids (e.g., lymph, serum, plasma, urine, synovial fluid and spinal fluid) or another tissue or cell sample taken from an individual having such a disorder, relative to the standard gene expression level, i.e., the expression level in healthy tissue or bodily fluid from an individual not having the disorder.

The tissue distribution in T-cells indicates that the protein product of this gene is useful for treatment and diagnosis of some immune disorders. Furthermore, this gene product may be involved in the regulation of cytokine production, antigen presentation, or other processes that may also suggest a usefulness in the treatment of cancer (e.g. by boosting immune responses). Since the gene is expressed in cells of lymphoid origin, the gene or protein, as well as, antibodies directed against the protein may show utility as a tumor marker and/or immunotherapy targets for the above listed tissues. Therefore it may be also used as an agent for immunological disorders including arthritis, asthma, immune deficiency diseases such as AIDS, leukemia, rheumatoid arthritis, inflammatory bowel disease, sepsis, acne, and psoriasis. In addition, this gene product may have commercial utility in the expansion of stem cells and committed progenitors of various blood lineages, and in the differentiation and/or proliferation of various cell types. Expression of this gene product in T cells also strongly indicates a role for this protein in immune function and immune surveillance. Protein, as well as, antibodies directed against the protein may show utility as a tumor marker and/or immunotherapy targets for the above listed tissues.

Many polynucleotide sequences, such as EST sequences, are publicly available and accessible through sequence databases. Some of these sequences are

related to SEQ ID NO:114 and may have been publicly available prior to conception of the present invention. Preferably, such related polynucleotides are specifically excluded from the scope of the present invention. To list every related sequence is cumbersome. Accordingly, preferably excluded from the present invention are one or more polynucleotides comprising a nucleotide sequence described by the general formula of a-b, where a is any integer between 1 to 689 of SEQ ID NO:114, b is an integer of 15 to 703, where both a and b correspond to the positions of nucleotide residues shown in SEQ ID NO:114, and where b is greater than or equal to a + 14.

FEATURES OF PROTEIN ENCODED BY GENE NO: 105

The translation product of this gene shares sequence homology with ARI protein of Drosophila (See Genbank Accession 2058299; EMBL: locus DMARIADNE, accession X98309), which is thought to be important in axonal path-finding in the central nervous system.

In specific embodiments, polypeptides of the invention comprise, or alternatively consists of, an amino acid sequence selected from the group: IREVNEVIQNPAT (SEQ ID NO:928), ITRILLSHFNWDKEKLMERYFDGNLEKLFA (SEQ ID NO:929), NTRSSAQDMPCQICYLNYPNSYF (SEQ ID NO:930), TGL ECGHKFCMQCWSEYLTTKIMEEGMGQTISCPAHG (SEQ ID NO:936), CDILVDDNTVMRLITDSKVKLKYQHLITNSFVECNRLLKWCPAPDCHHVVKV QYPDAKPV (SEQ ID NO:931), CDILVDDNTVMRLITDSKVKLKYQHLITNSFVECNRLLKWCPAPDCHHVVKV (SEQ ID NO:932), GCNHMVCRNQNCKAEFCWVCLGPWEPHGSAWYNCNRYNEDDAKAARDA QERSRAALQRYL (SEQ ID NO:933), FYCNRYMNHMQSLRFEHKLYAQVKQKMEEMQQHNMSWIEVQFLKKAVDV LCQCRATLMYT (SEQ ID NO:934), and/or YVFAFYLKKNNQSIIFENNQADLENATEVLSGYLERDISQDSLQDIKQKVQDK YRYCESR (SEQ ID NO:935). Moreover, fragments and variants of these

polypeptides (such as, for example, fragments as described herein, polypeptides at least 80%, 85%, 90%, 95%, 96%, 97%, 98%, or 99% identical to these polypeptides and polypeptides encoded by the polynucleotide which hybridizes, under stringent conditions, to the polynucleotide encoding these polypeptides) are encompassed by the invention. Antibodies that bind polypeptides of the invention are also encompassed by the invention. Polynucleotides encoding these polypeptides are also encompassed by the invention.

This gene is expressed primarily in adult brain, and to a lesser extent in testes, endometrial tumor, melanocytes, and infant brain.

Polynucleotides and polypeptides of the invention are useful as reagents for differential identification of the tissue(s) or cell type(s) present in a biological sample and for diagnosis of diseases and conditions which include, but are not limited to, diseases or injuries involving axonal path development. Similarly, polypeptides and antibodies directed to these polypeptides are useful in providing immunological probes for differential identification of the tissue(s) or cell type(s). For a number of disorders of the above tissues or cells, particularly of the central nervous system, expression of this gene at significantly higher or lower levels may be routinely detected in certain tissues or cell types (e.g. brain, testes, cancerous and wounded tissues) or bodily fluids (e.g., lymph, serum, plasma, urine, synovial fluid and spinal fluid) or another tissue or cell sample taken from an individual having such a disorder, relative to the standard gene expression level, i.e., the expression level in healthy tissue or bodily fluid from an individual not having the disorder.

The tissue distribution in adult brain, combined with the homology to ARI protein indicates that the protein product of this gene is useful for the treatment of disease states or injuries involving axonal path development, including neurodegenerative diseases and nerve injury, such as Alzheimer's Disease, Parkinson's Disease, Huntington's Disease, Tourette's Syndrome, schizophrenia, mania, dementia, paranoia, obsessive compulsive disorder, panic disorder, learning disabilities, ALS, psychoses, autism, and altered behaviors, including disorders in feeding, sleep patterns, balance, and perception. In addition, the gene or gene product may also play a role in the treatment and/or detection of developmental disorders associated with the developing embryo, or sexually-linked disorders. Protein, as well

as, antibodies directed against the protein may show utility as a tumor marker and/or immunotherapy targets for the above listed tissues.

Many polynucleotide sequences, such as EST sequences, are publicly available and accessible through sequence databases. Some of these sequences are related to SEQ ID NO:115 and may have been publicly available prior to conception of the present invention. Preferably, such related polynucleotides are specifically excluded from the scope of the present invention. To list every related sequence is cumbersome. Accordingly, preferably excluded from the present invention are one or more polynucleotides comprising a nucleotide sequence described by the general formula of a-b, where a is any integer between 1 to 3670 of SEQ ID NO:115, b is an integer of 15 to 3684, where both a and b correspond to the positions of nucleotide residues shown in SEQ ID NO:115, and where b is greater than or equal to a + 14.

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FEATURES OF PROTEIN ENCODED BY GENE NO: 106

The translation product of this gene shares sequence homology with cytochrome b561 [Sus scrofa] which is thought to be an integral membrane protein of neuroendocrine storage vesicles of neurotransmitters and peptide hormones. The gene encoding the disclosed cDNA is thought to reside on chromosome 11. Accordingly, polynucleotides related to this invention are useful as a marker in linkage analysis for chromosome 11.

This gene is expressed primarily in frontal cortex, and to a lesser extent in rhabdomyosarcoma.

Polynucleotides and polypeptides of the invention are useful as reagents for differential identification of the tissue(s) or cell type(s) present in a biological sample and for diagnosis of diseases and conditions which include, but are not limited to, neurological disorders. Similarly, polypeptides and antibodies directed to these polypeptides are useful in providing immunological probes for differential identification of the tissue(s) or cell type(s). For a number of disorders of the above tissues or cells, particularly of the central nervous system, expression of this gene at significantly higher or lower levels may be routinely detected in certain tissues or cell

types (e.g. brain, cancerous and wounded tissues) or bodily fluids (e.g., lymph, serum, plasma, urine, synovial fluid and spinal fluid) or another tissue or cell sample taken from an individual having such a disorder, relative to the standard gene expression level, i.e., the expression level in healthy tissue or bodily fluid from an individual not having the disorder.

Predicted epitopes include those comprising a sequence shown in SEQ ID NO: 354 as residues: Ser-18 to Pro-24.

The tissue distribution in frontal cortex, combined with the homology to cytochrome b561 [Sus scrofa] indicates that the protein product of this gene is useful for the treatment and diagnosis of neurological disorders. This gene may also be important in the regulation of some types of cancers. Furthermore, the tissue distribution indicates that the protein product of this gene is useful for the diagnosis and/or treatment of disorders of the brain and nervous system. Elevated expression of this gene product within the frontal cortex of the brain indicates that it may be involved in neuronal survival; synapse formation; conductance; neural differentiation, etc. Such involvement may impact many processes, such as learning and cognition. It may also be useful in the treatment of such neurodegenerative disorders as schizophrenia; ALS; or Alzheimer's.

Many polynucleotide sequences, such as EST sequences, are publicly available and accessible through sequence databases. Some of these sequences are related to SEQ ID NO:116 and may have been publicly available prior to conception of the present invention. Preferably, such related polynucleotides are specifically excluded from the scope of the present invention. To list every related sequence is cumbersome. Accordingly, preferably excluded from the present invention are one or more polynucleotides comprising a nucleotide sequence described by the general formula of a-b, where a is any integer between 1 to 1951 of SEQ ID NO:116, b is an integer of 15 to 1965, where both a and b correspond to the positions of nucleotide residues shown in SEQ ID NO:116, and where b is greater than or equal to a + 14.

FEATURES OF PROTEIN ENCODED BY GENE NO: 107

In specific embodiments, polypeptides of the invention comprise, or alternatively consists of, an amino acid sequence selected from the group: MWGYLFVDAAWNFLGCLICGW (SEQ ID NO:937), MHFISSGNVSAIRSSILLLRXSLSYLGNCLRVSAIFVYFLLFLLLS (SEQ ID NO:938), and/or MDQALRGSPSEGFSTDPSPPQVGRQIPSFPPWRRLVLPKASGCFLEREWWLCV FKLRTRPGAEAHAYNSSILGGRGKGIT (SEQ ID NO:939). Moreover, fragments and variants of these polypeptides (such as, for example, fragments as described herein, polypeptides at least 80%, 85%, 90%, 95%, 96%, 97%, 98%, or 99% identical to these polypeptides and polypeptides encoded by the polynucleotide which hybridizes, under stringent conditions, to the polynucleotide encoding these polypeptides) are encompassed by the invention. Antibodies that bind polypeptides of the invention are also encompassed by the invention. Polynucleotides encoding these polypeptides are also encompassed by the invention.

This gene is expressed primarily in pancreas tumor, and to a lesser extent in cerebellum.

Polynucleotides and polypeptides of the invention are useful as reagents for differential identification of the tissue(s) or cell type(s) present in a biological sample and for diagnosis of diseases and conditions which include, but are not limited to, pancreatic tumors. Similarly, polypeptides and antibodies directed to these polypeptides are useful in providing immunological probes for differential identification of the tissue(s) or cell type(s). For a number of disorders of the above tissues or cells, particularly of the endocrine system, expression of this gene at significantly higher or lower levels may be routinely detected in certain tissues or cell types (e.g. pancreas, cancerous and wounded tissues) or bodily fluids (e.g., lymph, serum, plasma, urine, synovial fluid and spinal fluid) or another tissue or cell sample taken from an individual having such a disorder, relative to the standard gene expression level, i.e., the expression level in healthy tissue or bodily fluid from an individual not having the disorder.

Predicted epitopes include those comprising a sequence shown in SEQ ID NO: 355 as residues: Pro-22 to Phe-33.

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The tissue distribution in pancreas tumors indicates that the protein product of this gene is useful for diagnosis and treatment of pancreatic tumors, and/or tumors of metabolic tissues and cell types. Protein, as well as, antibodies directed against the protein may show utility as a tumor marker and/or immunotherapy targets for the above listed tissues.

Many polynucleotide sequences, such as EST sequences, are publicly available and accessible through sequence databases. Some of these sequences are related to SEQ ID NO:117 and may have been publicly available prior to conception of the present invention. Preferably, such related polynucleotides are specifically excluded from the scope of the present invention. To list every related sequence is cumbersome. Accordingly, preferably excluded from the present invention are one or more polynucleotides comprising a nucleotide sequence described by the general formula of a-b, where a is any integer between 1 to 489 of SEQ ID NO:117, b is an integer of 15 to 503, where both a and b correspond to the positions of nucleotide residues shown in SEQ ID NO:117, and where b is greater than or equal to a + 14.

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FEATURES OF PROTEIN ENCODED BY GENE NO: 108

The gene encoding the disclosed cDNA is thought to reside on chromosome 17. Accordingly, polynucleotides related to this invention are useful as a marker in linkage analysis for chromosome 17.

In specific embodiments, polypeptides of the invention comprise, or alternatively consists of, an amino acid sequence selected from the group: MLPALASCCHFSPPEQAARLKKLQEQEKQQKVEFRKRMEKEVSDFIQDSGQI KKKFQPMNKIERSILHDVVEVAGLTSFSFGEDDDCRYVMIFKKEFAPSDEELD SYRRGEEWDPQKAEEKRNXKELAQRQ (SEQ ID NO:940), EEEAAQQGPVVVSPASDYKDKYSHLIGKGAAKDAAHMLQANKTYGCXPVA NKRDTRSIEEAMNEIRAKKRLRQSGE (SEQ ID NO:941), PPRRPAQLPLTPGAGQGAGRDKAAAIRAHPGAPPLNHLLP (SEQ ID NO:942), AVPQAGGKQVFDLSPLELGYVRGMCVCV (SEQ ID NO:943) and/or MLPALASCCHFSPPEQAARLKKLQEQEKQQKVEFRKRMEKEVSDFIQDSGQI

KKKFQPMNKIERSILHDVVEVAGLTSFSFGEDDDCRYVMIFKKEFAPSDEELD SYRRGEEWDPQKAEEKRNXKELAQRQEEEAAQQGPVVVSPASDYKDKYSHL IGKGAAKDAAHMLQANKTYGCXPVANKRDTRSIEEAMNEIRAKKRLRQSGE (SEQ ID NO:944). Moreover, fragments and variants of these polypeptides (such as, for example, fragments as described herein, polypeptides at least 80%, 85%, 90%, 95%, 96%, 97%, 98%, or 99% identical to these polypeptides and polypeptides encoded by the polynucleotide which hybridizes, under stringent conditions, to the polynucleotide encoding these polypeptides) are encompassed by the invention. Antibodies that bind polypeptides of the invention are also encompassed by the invention. Polynucleotides encoding these polypeptides are also encompassed by the invention.

The translation product of this gene shares sequence homology with FSA-1, which may play a role as a structural protein component of the acrosome. The mammalian spermatozoon undergoes continuous modifications during spermatogenesis, maturation in the epididymis, and capacitation in the female reproductive tract. Only the capacitated spermatozoa are capable of binding the zona-intact egg and undergoing the acrosome reaction. The fertilization process is a net result of multiple molecular events which enable ejaculated spermatozoa to recognize and bind to the egg's extracellular coat, the zona pellucida (ZP). Sperm-egg interaction is a species-specific event which is initiated by the recognition and binding of complementary molecule(s) present on sperm plasma membrane (receptor) and the surface of the ZP (ligand). This is a carbohydrate-mediated event which initiates a signal transduction cascade resulting in the exocytosis of acrosomal contents. This step is believed to be a prerequisite which enables the acrosome reacted spermatozoa to penetrate the ZP and fertilize the egg. Recently, another group published this gene, calling it sperm acrosomal protein [Homo sapiens] (Proc. Natl. Acad. Sci. U.S.A. 95 (14), 8175-8180 (1998)).

This gene is expressed primarily in fetal kidney and sperm.

Polynucleotides and polypeptides of the invention are useful as reagents for differential identification of the tissue(s) or cell type(s) present in a biological sample and for diagnosis of diseases and conditions which include, but are not limited to, male reproductive disorders, especially involving acrosomal dysfunction. Similarly,

polypeptides and antibodies directed to these polypeptides are useful in providing immunological probes for differential identification of the tissue(s) or cell type(s). For a number of disorders of the above tissues or cells, particularly of the male reproductive system, expression of this gene at significantly higher or lower levels may be routinely detected in certain tissues or cell types (e.g. sperm, cancerous and wounded tissues) or bodily fluids (e.g., lymph, serum, plasma, urine, synovial fluid and spinal fluid) or another tissue or cell sample taken from an individual having such a disorder, relative to the standard gene expression level, i.e., the expression level in healthy tissue or bodily fluid from an individual not having the disorder.

Predicted epitopes include those comprising a sequence shown in SEQ ID NO: 356 as residues: Met-12 to Gln-30, Lys-35 to Val-46, Arg-49 to Val-56, Gln-61 to Glu-77, Gly-96 to Cys-101, Glu-110 to Lys-139, Leu-141 to Gln-151, Ser-161 to Tyr-167, Asn-196 to Ile-203, Arg-211 to Ser-227.

The tissue distribution in sperm, combined with the homology to FSA-1 and the Homo sapiens sperm acrosomal protein indicates that the protein product of this gene is useful for the treatment of infertility due to acrosomal dysfunction of sperm. Protein may also be useful as a contraceptive either alone, or in combination with other therapies. Protein, as well as, antibodies directed against the protein may show utility as a tumor marker and/or immunotherapy targets for the above listed tissues.

Many polynucleotide sequences, such as EST sequences, are publicly available and accessible through sequence databases. Some of these sequences are related to SEQ ID NO:118 and may have been publicly available prior to conception of the present invention. Preferably, such related polynucleotides are specifically excluded from the scope of the present invention. To list every related sequence is cumbersome. Accordingly, preferably excluded from the present invention are one or more polynucleotides comprising a nucleotide sequence described by the general formula of a-b, where a is any integer between 1 to 1057 of SEQ ID NO:118, b is an integer of 15 to 1071, where both a and b correspond to the positions of nucleotide residues shown in SEQ ID NO:118, and where b is greater than or equal to a + 14.

FEATURES OF PROTEIN ENCODED BY GENE NO: 109

This gene is expressed primarily in pituitary tissue, and to a lesser extent in epididymus.

Polynucleotides and polypeptides of the invention are useful as reagents for differential identification of the tissue(s) or cell type(s) present in a biological sample and for diagnosis of diseases and conditions which include, but are not limited to, male reproductive disorders. Similarly, polypeptides and antibodies directed to these polypeptides are useful in providing immunological probes for differential identification of the tissue(s) or cell type(s). For a number of disorders of the above tissues or cells, particularly of the male reproductive system, expression of this gene at significantly higher or lower levels may be routinely detected in certain tissues or cell types (e.g. epididymus, cancerous and wounded tissues) or bodily fluids (e.g., lymph, serum, plasma, urine, synovial fluid and spinal fluid) or another tissue or cell sample taken from an individual having such a disorder, relative to the standard gene expression level, i.e., the expression level in healthy tissue or bodily fluid from an individual not having the disorder.

Predicted epitopes include those comprising a sequence shown in SEQ ID NO: 357 as residues: Met-1 to Trp-6.

Because the gene is found in both pituitary and epididymus, this indicates that the protein product of this gene is useful for the treatment and diagnosis of male reproductive disorders. This may involve a secreted peptide produced in the pituitary targeting the epididymus. Protein, as well as, antibodies directed against the protein may show utility as a tumor marker and/or immunotherapy targets for the above listed tissues.

Many polynucleotide sequences, such as EST sequences, are publicly available and accessible through sequence databases. Some of these sequences are related to SEQ ID NO:119 and may have been publicly available prior to conception of the present invention. Preferably, such related polynucleotides are specifically excluded from the scope of the present invention. To list every related sequence is cumbersome. Accordingly, preferably excluded from the present invention are one or more polynucleotides comprising a nucleotide sequence described by the general formula of a-b, where a is any integer between 1 to 1087 of SEQ ID NO:119, b is an

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integer of 15 to 1101, where both a and b correspond to the positions of nucleotide residues shown in SEQ ID NO:119, and where b is greater than or equal to a + 14.

FEATURES OF PROTEIN ENCODED BY GENE NO: 110

In specific embodiments, polypeptides of the invention comprise, or alternatively consists of, an amino acid sequence selected from the group: LLCPVLNSGXSWNFPHPSQPEYSFHGFHSTRLWI (SEQ ID NO:945), and/or PSTPWFLFLLGLTCPFSTSHPRWDSIPP (SEQ ID NO:946). Moreover, fragments and variants of these polypeptides (such as, for example, fragments as described herein, polypeptides at least 80%, 85%, 90%, 95%, 96%, 97%, 98%, or 99% identical to these polypeptides and polypeptides encoded by the polynucleotide which hybridizes, under stringent conditions, to the polynucleotide encoding these polypeptides) are encompassed by the invention. Antibodies that bind polypeptides of the invention are also encompassed by the invention. Polynucleotides encoding these polypeptides are also encompassed by the invention.

This gene is expressed primarily in resting T-cells. .

Polynucleotides and polypeptides of the invention are useful as reagents for differential identification of the tissue(s) or cell type(s) present in a biological sample and for diagnosis of diseases and conditions which include, but are not limited to, T-cell disorders. Similarly, polypeptides and antibodies directed to these polypeptides are useful in providing immunological probes for differential identification of the tissue(s) or cell type(s). For a number of disorders of the above tissues or cells, particularly of the immune system, expression of this gene at significantly higher or lower levels may be routinely detected in certain tissues or cell types (e.g. immune, cancerous and wounded tissues) or bodily fluids (e.g., lymph, serum, plasma, urine, synovial fluid and spinal fluid) or another tissue or cell sample taken from an individual having such a disorder, relative to the standard gene expression level, i.e., the expression level in healthy tissue or bodily fluid from an individual not having the disorder.

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The tissue distribution in T-cells indicates that the protein product of this gene is useful for the treatment and diagnosis of certain immune disorders, especially those involving T-cells. Furthermore, this gene product may be involved in the regulation of cytokine production, antigen presentation, or other processes that may also suggest a usefulness in the treatment of cancer (e.g. by boosting immune responses). Since the gene is expressed in cells of lymphoid origin, the gene or protein, as well as, antibodies directed against the protein may show utility as a tumor marker and/or immunotherapy targets for the above listed tissues. Therefore it may be also used as an agent for immunological disorders including arthritis, asthma, immune deficiency diseases such as AIDS, leukemia, rheumatoid arthritis, inflammatory bowel disease, sepsis, acne, and psoriasis. In addition, this gene product may have commercial utility in the expansion of stem cells and committed progenitors of various blood lineages, and in the differentiation and/or proliferation of various cell types. Expression of this gene product in T cells also strongly indicates a role for this protein in immune function and immune surveillance. Protein, as well as, antibodies directed against the protein may show utility as a tumor marker and/or immunotherapy targets for the above listed tissues.

Many polynucleotide sequences, such as EST sequences, are publicly available and accessible through sequence databases. Some of these sequences are related to SEQ ID NO:120 and may have been publicly available prior to conception of the present invention. Preferably, such related polynucleotides are specifically excluded from the scope of the present invention. To list every related sequence is cumbersome. Accordingly, preferably excluded from the present invention are one or more polynucleotides comprising a nucleotide sequence described by the general formula of a-b, where a is any integer between 1 to 268 of SEQ ID NO:120, b is an integer of 15 to 282, where both a and b correspond to the positions of nucleotide residues shown in SEQ ID NO:120, and where b is greater than or equal to a + 14.

FEATURES OF PROTEIN ENCODED BY GENE NO: 111

The gene encoding the disclosed cDNA is thought to reside on chromosome 10. Accordingly, polynucleotides related to this invention are useful as a marker in linkage analysis for chromosome 10.

This gene is expressed primarily in cerebellum and whole brain, and to a lesser extent in infant brain and fetal kidney.

Polynucleotides and polypeptides of the invention are useful as reagents for differential identification of the tissue(s) or cell type(s) present in a biological sample and for diagnosis of diseases and conditions which include, but are not limited to, neurological disorders. Similarly, polypeptides and antibodies directed to these polypeptides are useful in providing immunological probes for differential identification of the tissue(s) or cell type(s). For a number of disorders of the above tissues or cells, particularly of the central nervous system, expression of this gene at significantly higher or lower levels may be routinely detected in certain tissues or cell types (e.g. brain, cancerous and wounded tissues) or bodily fluids (e.g., lymph, serum, plasma, urine, synovial fluid and spinal fluid) or another tissue or cell sample taken from an individual having such a disorder, relative to the standard gene expression level, i.e., the expression level in healthy tissue or bodily fluid from an individual not having the disorder.

Predicted epitopes include those comprising a sequence shown in SEQ ID NO: 359 as residues: Asp-48 to Gly-55.

The tissue distribution in cerebellum and whole brain indicates that the protein product of this gene is useful for diagnosis and treatment of neurological disorders, such as Alzheimer's Disease, Parkinson's Disease, Huntington's Disease, Tourette's Syndrome, schizophrenia, mania, dementia, paranoia, obsessive compulsive disorder, panic disorder, learning disabilities, ALS, psychoses, autism, and altered behaviors, including disorders in feeding, sleep patterns, balance, and perception. In addition, the gene or gene product may also play a role in the treatment and/or detection of developmental disorders associated with the developing embryo, or sexually-linked disorders. Protein, as well as, antibodies directed against the protein may show utility as a tumor marker and/or immunotherapy targets for the above listed tissues.

Many polynucleotide sequences, such as EST sequences, are publicly available and accessible through sequence databases. Some of these sequences are

related to SEQ ID NO:121 and may have been publicly available prior to conception of the present invention. Preferably, such related polynucleotides are specifically excluded from the scope of the present invention. To list every related sequence is cumbersome. Accordingly, preferably excluded from the present invention are one or more polynucleotides comprising a nucleotide sequence described by the general formula of a-b, where a is any integer between 1 to 2621 of SEQ ID NO:121, b is an integer of 15 to 2635, where both a and b correspond to the positions of nucleotide residues shown in SEQ ID NO:121, and where b is greater than or equal to a + 14.

FEATURES OF PROTEIN ENCODED BY GENE NO: 112

The translation product of this gene shares sequence homology with yeast mitochondrial ribosomal protein, which is homologous to ribosomal protein s15 of *E.coli*, which is thought to be important in the early assembly of ribosomes (See Genbank Accession No. M38016). The gene encoding the disclosed cDNA is thought to reside on chromosome 1. Accordingly, polynucleotides related to this invention are useful as a marker in linkage analysis for chromosome 1.

This gene is expressed primarily in developmental tissues.

Polynucleotides and polypeptides of the invention are useful as reagents for differential identification of the tissue(s) or cell type(s) present in a biological sample and for diagnosis of diseases and conditions which include, but are not limited to, development of cancers and tumors in addition to healing wounds. Similarly, polypeptides and antibodies directed to these polypeptides are useful in providing immunological probes for differential identification of the tissue(s) or cell type(s). For a number of disorders of the above tissues or cells, particularly of the immune and developmental systems, expression of this gene at significantly higher or lower levels may be routinely detected in certain tissues or cell types (e.g. developmental, cancerous and wounded tissues) or bodily fluids (e.g., lymph, serum, plasma, urine, synovial fluid and spinal fluid) or another tissue or cell sample taken from an individual having such a disorder, relative to the standard gene expression level, i.e.,

the expression level in healthy tissue or bodily fluid from an individual not having the disorder.

The tissue distribution in developmental tissues, combined with the homology to ribosomal protein s15 of E. coli indicates that the protein product of this gene is useful for the diagnosis and/or treatment of diseases related to the assembly of ribosomes in the mitochondria, which is important in the translation of RNA into protein. Therefore, this indicates that the protein product of this gene is also useful for the diagnosis and intervention of multiple tumors, as well as in healing wounds, which are thought to be under similar regulation as developmental tissues. Protein, as well as, antibodies directed against the protein have utility as tumor markers, in addition to immunotherapy targets, for the above listed tumors and tissues.

Many polynucleotide sequences, such as EST sequences, are publicly available and accessible through sequence databases. Some of these sequences are related to SEQ ID NO:122 and may have been publicly available prior to conception of the present invention. Preferably, such related polynucleotides are specifically excluded from the scope of the present invention. To list every related sequence is cumbersome. Accordingly, preferably excluded from the present invention are one or more polynucleotides comprising a nucleotide sequence described by the general formula of a-b, where a is any integer between 1 to 980 of SEQ ID NO:122, b is an integer of 15 to 994, where both a and b correspond to the positions of nucleotide residues shown in SEQ ID NO:122, and where b is greater than or equal to a + 14.

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FEATURES OF PROTEIN ENCODED BY GENE NO: 113

For purposes of this application, this gene and its corresponding translation product are known as the B7-H4 gene and B7-H4 protein. This protein is believed to reside as a cell-surface molecule, and the transmembrane domain of this protein is believed to embody the following preferred amino acid residues: GIVAFIVFLLLIMLIFL (SEQ ID NO: 1236). Polynucleotides encoding this polypeptide are also encompassed by the invention, as are antibodies that bind the polypeptide. The B7-H4 gene shares sequence homology with members of the B7

family of ligands (i.e., B7-1 (See Genbank Accession 507873)). These proteins and their corresponding receptors play vital roles in the growth, differentiation and death of T cells. For example, some members of this family (i.e., B7-H1) are involved in costimulation of the T cell response, as well as inducing increased cytokine production. Therefore, agonists and/or antagonists such as antibodies or small molecules directed against the B7-H4 gene are useful for treating T cell mediated immune system disorders. The gene encoding the disclosed cDNA is thought to reside on chromosome 1. Accordingly, polynucleotides related to this invention have uses, such as, for example, as a marker in linkage analysis for chromosome 1.

The translation product of this gene shares sequence homology with human poliovirus receptor precursors which are thought to be important in viral binding and uptake. The translation product of this gene also shares homology with a mouse member of the immunoglobulin superfamily, which is thought to be important in proper immune function (GENBANK: accession AF061260).

In specific embodiments, polypeptides of the invention comprise, or alternatively consists of, an amino acid sequence selected from the group: ELSISISNVALADEGEYTCSIFTMPVRTAKSLVTVLGIPQKPIITGYKSSLREKD TATLNCQSSGSKPAARLTWRKGDQELHGEPTRIQEDPNGKTFTVSSSVTFQVT REDDGASIVCSVNHESLKGADRSTSQRIEVLYTPTAMIRPDPPHPREGQKLLL HCEGRGNPVPQQYLWEKEGSVPPLKMTQESALIFPFLNKSDSGTYGCTATSN MGSYKAYYTLNVND (SEQ ID NO:947), ELSISISNVALADEGEYTCSIFTMPVRTAKSLVTVLGIPQKPIITGYKSSLREKD TATLNCQSS (SEQ ID NO:948), CQSSGSKPAARLTWRKGDQELHGEPTRIQEDPNGKTFTVSSSVTFQVTREDD GASIVCSVNHESL (SEQ ID NO:949), HESLKGADRSTSQRIEVLYTPTAMIRPDPPHPREGQKLLLHCEGRGNPVPQQY LWEKE (SEQ ID NO:950), WEKEGSVPPLKMTQESALIFPFLNKSDSGTYGCTATSNMGSYKAYYTLNVND (SEQ ID NO:951), PSPVPSSSSTYHAIIGGIVAFIVFLLLIMLIFLGHY (SEQ ID NO:952), and/or LIRHKGTYLTHEAKGSDDAPDADTAIINAEGGQSGGDDKK EYFI (SEQ ID NO:953). Moreover, fragments and variants of these polypeptides (such as, for example, fragments as described herein, polypeptides at least 80%, 85%,

90%, 95%, 96%, 97%, 98%, or 99% identical to these polypeptides and polypeptides encoded by the polynucleotide which hybridizes, under stringent conditions, to the polynucleotide encoding these polypeptides) are encompassed by the invention. Antibodies that bind polypeptides of the invention are also encompassed by the invention. Polynucleotides encoding these polypeptides are also encompassed by the invention.

A splice variant of this gene has been identified which encodes a polypeptide lacking the following amino acid segment of SEQ ID NO: 361: DGYWQEQDLELGTLAPLDEAISSTWSSPDMLASQ (SEQ ID NO: 1240). This splice variant was identified in clone HCE1K47, deposited in ATCC Deposit Accession No. PTA-2574 on October 5, 2000 and in ATCC Deposit Accession No. PTA-3070 on February 16, 2001.

In specific embodiments, polypeptides of the invention comprise, or alternatively consists of, an amino acid sequence selected from the group: NLSQDGYWQEQDLELGTLAPLDEAISSTWSSPDMLASQDSQP (SEQ ID NO: 1241), DGYWQEQDLELGTLAPLDEAISSTWSSPDMLASQ (SEQ ID NO: 1240), and/or NLSQDSQP (SEQ ID NO: 1242). In a further specific embodiment, polypeptides of the invention comprise, or alternatively consist of, the following amino acid sequence: MGAPAASLLLLLLLFACCWAPGGANLSQDDSQPWTSDETVVAGGTVVLKCQ VKDHEDSSLQWS (SEQ ID NO: 1243). Moreover, fragments and variants of these polypeptides (such as, for example, fragments as described herein, polypeptides at least 80%, 85%, 90%, 95%, 96%, 97%, 98%, or 99% identical to these polypeptides and polypeptides encoded by the polynucleotide which hybridizes, under stringent conditions, to the polynucleotide encoding these polypeptides) are encompassed by the invention. Antibodies that bind polypeptides of the invention are also encompassed by the invention. Polynucleotides encoding these polypeptides are also encompassed by the invention.

It has been discovered that this gene is expressed almost exclusively in human brain tissue.

Preferred polypeptides of the present invention comprise, or alternatively consist of, one, two, three, four, five, six, seven, eight, nine, ten, eleven, twelve,

1-0-0-3-5-0-2-0-0-2-0-0-1-0

thirteen, fourteen, fifteen, sixteen, or all sixteen of the immunogenic epitopes of the extracellular portion of the B7-H4 protein shown in SEQ ID NO: 361 as residues: Leu-26 to Asp-36, Gln-63 to Asp-71, Lys-87 to Gln-102, Gly-107 to Arg-116, Tyr-172 to Ala-182, Thr-198 to His-207, Glu-209 to Lys-220, Thr-233 to Gly-238, Glu-248 to Gln-259, Pro-273 to Gln-282, Glu-289 to Gln-297, Asn-324 to Thr-330, Val-350 to Pro-355, Ile-390 to Thr-395, Ala-401 to Ala-410, Glu-418 to Tyr-430. Polynucleotides encoding these polypeptides are also encompassed by the invention, as are antibodies that bind one or more of these peptides.

In additional nonexclusive embodiments, polypeptides of the invention comprise, or alternatively consist of, one or more of the following amino acid sequences:

1.) The extracellular domain of the B7-H4 protein:

MGAPAASLLLLLLLFACCWAPGGANLSQDGYWQEQDLELGTLAPLDEAISST WSSPDMLASQDSQPWTSDETVVAGGTVVLKCQVKDHEDSSLQWSNPAQQT LYFGEKRALRDNRIQLVTSTPHELSISISNVALADEGEYTCSIFTMPVRTAKSL VTVLGIPQKPIITGYKSSLREKDTATLNCQSSGSKPAARLTWRKGDQELHGEP TRIQEDPNGKTFTVSSSVTFQVTREDDGASIVCSVNHESLKGADRSTSQRIEVL YTPTAMIRPDPPHPREGQKLLLHCEGRGNPVPQQYLWEKEGSVPPLKMTQES ALIFPFLNKSDSGTYGCTATSNMGSYKAYYTLNVNDPSPVPSSSSTYHAIIG (SEQ ID NO: 1237);

2.) The mature extracellular domain of the B7-H4 protein:

NLSQDGYWQEQDLELGTLAPLDEAISSTVWSSPDMLASQDSQPWTSDETVV AGGTVVLKCQVKDHEDSSLQWSNPAQQTLYFGEKRALRDNRIQLVTSTPHEL SISISNVALADEGEYTCSIFTMPVRTAKSLVTVLGIPQKPIITGYKSSLREKDTA TLNCQSSGSKPAARLTWRKGDQELHGEPTRIQEDPNGKTFTVSSSVTFQVTRE DDGASIVCSVNHESLKGADRSTSQRIEVLYTPTAMIRPDPPHPREGQKLLLHC EGRGNPVPQQYLWEKEGSVPPLKMTQESALIFPFLNKSDSGTYGCTATSNMG SYKAYYTLNVNDPSPVPSSSSTYHAIIG (SEQ ID NO: 1238); and/or

3.) The anticipated leader sequence of the B7-H4 protein:

MGAPAASLLLLLLLFACCWAPGGA (SEQ ID NO: 1239).

Polynucleotides encoding these polypeptides are also encompassed by the invention, as are antibodies that bind one or more of these polypeptides.

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Also preferred are polypeptides comprising, or alternatively consisting of, fragments of the mature extracellular portion of the B7-H4 protein demonstrating functional activity (SEQ ID NO: 361). Polynucleotides encoding these polypeptides are also encompassed by the invention. By functional activity is meant, a polypeptide fragment capable of displaying one or more known functional activities associated with the full-length (complete) B7-H4 protein. Such functional activities include, but are not limited to, biological activity (e.g., T cell costimulatory activity, ability to bind ICOS, and ability to induce or inhibit cytokine production), antigenicity [ability to bind (or compete with a B7-H4 polypeptide for binding) to an anti-B7-H4 antibody], immunogenicity (ability to generate antibody which binds to a B7-H4 polypeptide), ability to form multimers with B7-H4 polypeptides of the invention, and ability to bind to a receptor or ligand for a B7-H4 polypeptide.

Figures 3A-C show the nucleotide (SEQ ID NO: 123) and deduced amino acid sequence (SEQ ID NO: 361) corresponding to this gene.

Figure 4 shows an analysis of the amino acid sequence (SEQ ID NO: 361). Alpha, beta, turn and coil regions; hydrophilicity and hydrophobicity; amphipathic regions; flexible regions; antigenic index and surface probability are shown, and all were generated using the default settings of the recited computer algorithms. In the "Antigenic Index or Jameson-Wolf" graph, the positive peaks indicate locations of the highly antigenic regions of the protein, i.e., regions from which epitope-bearing peptides of the invention can be obtained. Polypeptides comprising, or alternatively consisting of, domains defined by these graphs are contemplated by the present invention, as are polynucleotides encoding these polypeptides.

The data presented in Figure 4 are also represented in tabular form in Table 4. The columns are labeled with the headings "Res", "Position", and Roman Numerals I-XIV. The column headings refer to the following features of the amino acid sequence presented in Figures 3A-3C, and Table 4: "Res": amino acid residue of SEQ ID NO: 361 and Figures 3A-3C; "Position": position of the corresponding residue within SEQ ID NO: 361 and Figures 3A-3C; I: Alpha, Regions - Garnier-Robson; II: Alpha, Regions - Chou-Fasman; III: Beta, Regions - Garnier-Robson; IV: Beta, Regions - Chou-Fasman; V: Turn, Regions - Garnier-Robson; VI: Turn, Regions - Chou-Fasman; VII: Coil, Regions - Garnier-Robson; VIII: Hydrophilicity Plot - Kyte-

Doolittle; IX: Hydrophobicity Plot - Hopp-Woods; X: Alpha, Amphipathic Regions - Eisenberg; XI: Beta, Amphipathic Regions - Eisenberg; XII: Flexible Regions - Karplus-Schulz; XIII: Antigenic Index - Jameson-Wolf; and XIV: Surface Probability Plot - Emini.

Preferred embodiments of the invention in this regard include fragments that comprise, or alternatively consisting of, one or more of the following regions: alpha-helix and alpha-helix forming regions ("alpha-regions"), beta-sheet and beta-sheet forming regions ("beta-regions"), turn and turn-forming regions ("turn-regions"), coil and coil-forming regions ("coil-regions"), hydrophilic regions, hydrophobic regions, alpha amphipathic regions, beta amphipathic regions, flexible regions, surface-forming regions and high antigenic index regions. The data representing the structural or functional attributes of the protein set forth in Figure 4 and/or Table 4, as described above, was generated using the various modules and algorithms of the DNA*STAR set on default parameters. In a preferred embodiment, the data presented in columns VIII, IX, XIII, and XIV of Table 4 can be used to determine regions of the protein which exhibit a high degree of potential for antigenicity. Regions of high antigenicity are determined from the data presented in columns VIII, IX, XIII, and/or XIV by choosing values which represent regions of the polypeptide which are likely to be exposed on the surface of the polypeptide in an environment in which antigen recognition may occur in the process of initiation of an immune response.

Certain preferred regions in these regards are set out in Figure 4, but may, as shown in Table 4, be represented or identified by using tabular representations of the data presented in Figure 4. The DNA*STAR computer algorithm used to generate Figure 4 (set on the original default parameters) was used to present the data in Figure 4 in a tabular format (See Table 4). The tabular format of the data in Figure 4 is used to easily determine specific boundaries of a preferred region.

The present invention is further directed to fragments of the polynucleotide sequences described herein. By a fragment of, for example, the polynucleotide sequence of a deposited cDNA or the nucleotide sequence shown in SEQ ID NO: 123, is intended polynucleotide fragments at least about 15nt, and more preferably at least about 20 nt, at least about 25nt, still more preferably at least about 30 nt, at least

about 35nt, and even more preferably, at least about 40 nt in length, at least about 45nt in length, at least about 50nt in length, at least about 60nt in length, at least about 70nt in length, at least about 80nt in length, at least about 90nt in length, at least about 100nt in length, at least about 125nt in length, at least about 150nt in length, at least about 175nt in length, which are useful as diagnostic probes and primers as discussed herein. Of course, larger fragments 200-1500 nt in length are also useful according to the present invention, as are fragments corresponding to most, if not all, of the nucleotide sequence of a deposited cDNA or as shown in SEQ ID NO: 123. By a fragment at least 20 nt in length, for example, is intended fragments which include 20 or more contiguous bases from the nucleotide sequence of a deposited cDNA or the nucleotide sequence as shown in SEQ ID NO: 123. In this context "about" includes the particularly recited size, an sizes larger or smaller by several (5, 4, 3, 2, or 1) nucleotides, at either terminus or at both termini. Representative examples of polynucleotide fragments of the invention include, for example, fragments that comprise, or alternatively, consist of, a sequence from about nucleotide 1 to about 50, from about 51 to about 100, from about 101 to about 150, from about 151 to about 200, from about 201 to about 250, from about 251 to about 300, from about 301 to about 350, from about 351 to about 400, from about 401 to about 450, from about 451 to about 500, and from about 501 to about 550, and from about 551 to about 600, from about 601 to about 650, from about 651 to about 700, from about 701 to about 750, from about 751 to about 800, and from about 801 to about 860, of SEQ ID NO: 123, or the complementary strand thereto, or the cDNA contained in a deposited clone. In this context "about" includes the particularly recited ranges, and ranges larger or smaller by several (5, 4, 3, 2, or 1) nucleotides, at either terminus or at both termini. In additional embodiments, the polynucleotides of the invention encode functional attributes of the corresponding protein.

Preferred polypeptide fragments of the invention comprise, or alternatively consist of, the secreted protein having a continuous series of deleted residues from the amino or the carboxyl terminus, or both. Particularly, N-terminal deletions of the polypeptide can be described by the general formula m-432 where m is an integer from 2 to 426, where m corresponds to the position of the amino acid residue identified in SEQ ID NO: 361. More in particular, the invention provides

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polynucleotides encoding polypeptides comprising, or alternatively consisting of, an amino acid sequence selected from the group: G-2 to I-432; A-3 to I-432; P-4 to I-432; A-5 to I-432; A-6 to I-432; S-7 to I-432; L-8 to I-432; L-9 to I-432; L-10 to I-432; L-11 to I-432; L-12 to I-432; L-13 to I-432; L-14 to I-432; F-15 to I-432; A-16 to I-432; C-17 to I-432; C-18 to I-432; W-19 to I-432; A-20 to I-432; P-21 to I-432; G-22 to I-432; G-23 to I-432; A-24 to I-432; N-25 to I-432; L-26 to I-432; S-27 to I-432; Q-28 to I-432; D-29 to I-432; G-30 to I-432; Y-31 to I-432; W-32 to I-432; Q-33 to I-432; E-34 to I-432; Q-35 to I-432; D-36 to I-432; L-37 to I-432; E-38 to I-432; L-39 to I-432; G-40 to I-432; T-41 to I-432; L-42 to I-432; A-43 to I-432; P-44 to I-432; L-45 to I-432; D-46 to I-432; E-47 to I-432; A-48 to I-432; I-49 to I-432; S-50 to I-432; S-51 to I-432; T-52 to I-432; V-53 to I-432; W-54 to I-432; S-55 to I-432; S-56 to I-432; P-57 to I-432; D-58 to I-432; M-59 to I-432; L-60 to I-432; A-61 to I-432; S-62 to I-432; Q-63 to I-432; D-64 to I-432; S-65 to I-432; Q-66 to I-432; P-67 to I-432; W-68 to I-432; T-69 to I-432; S-70 to I-432; D-71 to I-432; E-72 to I-432; T-73 to I-432; V-74 to I-432; V-75 to I-432; A-76 to I-432; G-77 to I-432; G-78 to I-432; T-79 to I-432; V-80 to I-432; V-81 to I-432; L-82 to I-432; K-83 to I-432; C-84 to I-432; Q-85 to I-432; V-86 to I-432; K-87 to I-432; D-88 to I-432; H-89 to I-432; E-90 to I-432; D-91 to I-432; S-92 to I-432; S-93 to I-432; L-94 to I-432; Q-95 to I-432; W-96 to I-432; S-97 to I-432; N-98 to I-432; P-99 to I-432; A-100 to I-432; Q-101 to I-432; Q-102 to I-432; T-103 to I-432; L-104 to I-432; Y-105 to I-432; F-106 to I-432; G-107 to I-432; E-108 to I-432; K-109 to I-432; R-110 to I-432; A-111 to I-432; L-112 to I-432; R-113 to I-432; D-114 to I-432; N-115 to I-432; R-116 to I-432; I-117 to I-432; Q-118 to I-432; L-119 to I-432; V-120 to I-432; T-121 to I-432; S-122 to I-432; T-123 to I-432; P-124 to I-432; H-125 to I-432; E-126 to I-432; L-127 to I-432; S-128 to I-432; I-129 to I-432; S-130 to I-432; I-131 to I-432; S-132 to I-432; N-133 to I-432; V-134 to I-432; A-135 to I-432; L-136 to I-432; A-137 to I-432; D-138 to I-432; E-139 to I-432; G-140 to I-432; E-141 to I-432; Y-142 to I-432; T-143 to I-432; C-144 to I-432; S-145 to I-432; I-146 to I-432; F-147 to I-432; T-148 to I-432; M-149 to I-432; P-150 to I-432; V-151 to I-432; R-152 to I-432; T-153 to I-432; A-154 to I-432; K-155 to I-432; S-156 to I-432; L-157 to I-432; V-158 to I-432; T-159 to I-432; V-160 to I-432; L-161 to I-432; G-162 to I-432; I-163 to I-432; P-164 to I-432; Q-165 to I-432; K-166 to I-432; P-167 to I-432; I-168 to I-432; I-169 to I-432;

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T-170 to I-432; G-171 to I-432; Y-172 to I-432; K-173 to I-432; S-174 to I-432; S-175 to I-432; L-176 to I-432; R-177 to I-432; E-178 to I-432; K-179 to I-432; D-180 to I-432; T-181 to I-432; A-182 to I-432; T-183 to I-432; L-184 to I-432; N-185 to I-432; C-186 to I-432; Q-187 to I-432; S-188 to I-432; S-189 to I-432; G-190 to I-432; S-191 to I-432; K-192 to I-432; P-193 to I-432; A-194 to I-432; A-195 to I-432; R-196 to I-432; L-197 to I-432; T-198 to I-432; W-199 to I-432; R-200 to I-432; K-201 to I-432; G-202 to I-432; D-203 to I-432; Q-204 to I-432; E-205 to I-432; L-206 to I-432; H-207 to I-432; G-208 to I-432; E-209 to I-432; P-210 to I-432; T-211 to I-432; R-212 to I-432; I-213 to I-432; Q-214 to I-432; E-215 to I-432; D-216 to I-432; P-217 to I-432; N-218 to I-432; G-219 to I-432; K-220 to I-432; T-221 to I-432; F-222 to I-432; T-223 to I-432; V-224 to I-432; S-225 to I-432; S-226 to I-432; S-227 to I-432; V-228 to I-432; T-229 to I-432; F-230 to I-432; Q-231 to I-432; V-232 to I-432; T-233 to I-432; R-234 to I-432; E-235 to I-432; D-236 to I-432; D-237 to I-432; G-238 to I-432; A-239 to I-432; S-240 to I-432; I-241 to I-432; V-242 to I-432; C-243 to I-432; S-244 to I-432; V-245 to I-432; N-246 to I-432; H-247 to I-432; E-248 to I-432; S-249 to I-432; L-250 to I-432; K-251 to I-432; G-252 to I-432; A-253 to I-432; D-254 to I-432; R-255 to I-432; S-256 to I-432; T-257 to I-432; S-258 to I-432; Q-259 to I-432; R-260 to I-432; I-261 to I-432; E-262 to I-432; V-263 to I-432; L-264 to I-432; Y-265 to I-432; T-266 to I-432; P-267 to I-432; T-268 to I-432; A-269 to I-432; M-270 to I-432; I-271 to I-432; R-272 to I-432; P-273 to I-432; D-274 to I-432; P-275 to I-432; P-276 to I-432; H-277 to I-432; P-278 to I-432; R-279 to I-432; E-280 to I-432; G-281 to I-432; Q-282 to I-432; K-283 to I-432; L-284 to I-432; L-285 to I-432; L-286 to I-432; H-287 to I-432; C-288 to I-432; E-289 to I-432; G-290 to I-432; R-291 to I-432; G-292 to I-432; N-293 to I-432; P-294 to I-432; V-295 to I-432; P-296 to I-432; Q-297 to I-432; Q-298 to I-432; Y-299 to I-432; L-300 to I-432; W-301 to I-432; E-302 to I-432; K-303 to I-432; E-304 to I-432; G-305 to I-432; S-306 to I-432; V-307 to I-432; P-308 to I-432; P-309 to I-432; L-310 to I-432; K-311 to I-432; M-312 to I-432; T-313 to I-432; Q-314 to I-432; E-315 to I-432; S-316 to I-432; A-317 to I-432; L-318 to I-432; I-319 to I-432; F-320 to I-432; P-321 to I-432; F-322 to I-432; L-323 to I-432; N-324 to I-432; K-325 to I-432; S-326 to I-432; D-327 to I-432; S-328 to I-432; G-329 to I-432; T-330 to I-432; Y-331 to I-432; G-332 to I-432; C-333 to I-432; T-334 to I-432; A-335 to I-432; T-336 to I-432; S-337 to I-432; N-

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338 to I-432; M-339 to I-432; G-340 to I-432; S-341 to I-432; Y-342 to I-432; K-343 to I-432; A-344 to I-432; Y-345 to I-432; Y-346 to I-432; T-347 to I-432; L-348 to I-432; N-349 to I-432; V-350 to I-432; N-351 to I-432; D-352 to I-432; P-353 to I-432; S-354 to I-432; P-355 to I-432; V-356 to I-432; P-357 to I-432; S-358 to I-432; S-359 to I-432; S-360 to I-432; S-361 to I-432; T-362 to I-432; Y-363 to I-432; H-364 to I-432; A-365 to I-432; I-366 to I-432; I-367 to I-432; G-368 to I-432; G-369 to I-432; I-370 to I-432; V-371 to I-432; A-372 to I-432; F-373 to I-432; I-374 to I-432; V-375 to I-432; F-376 to I-432; L-377 to I-432; L-378 to I-432; L-379 to I-432; I-380 to I-432; M-381 to I-432; L-382 to I-432; I-383 to I-432; F-384 to I-432; L-385 to I-432; G-386 to I-432; H-387 to I-432; Y-388 to I-432; L-389 to I-432; I-390 to I-432; R-391 to I-432; H-392 to I-432; K-393 to I-432; G-394 to I-432; T-395 to I-432; Y-396 to I-432; L-397 to I-432; T-398 to I-432; H-399 to I-432; E-400 to I-432; A-401 to I-432; K-402 to I-432; G-403 to I-432; S-404 to I-432; D-405 to I-432; D-406 to I-432; A-407 to I-432; P-408 to I-432; D-409 to I-432; A-410 to I-432; D-411 to I-432; T-412 to I-432; A-413 to I-432; I-414 to I-432; I-415 to I-432; N-416 to I-432; A-417 to I-432; E-418 to I-432; G-419 to I-432; G-420 to I-432; Q-421 to I-432; S-422 to I-432; G-423 to I-432; G-424 to I-432; D-425 to I-432; D-426 to I-432; and/or K-427 to I-432 of SEQ ID NO: 361. Polypeptides encoded by these polynucleotides are also encompassed by the invention.

Additionally, the invention provides polynucleotides encoding polypeptides comprising, or alternatively consisting of, an amino acid sequence selected from the following group of C-terminal deletions: M-1 to F-431; M-1 to Y-430; M-1 to E-429; M-1 to K-428; M-1 to K-427; M-1 to D-426; M-1 to D-425; M-1 to G-424; M-1 to G-423; M-1 to S-422; M-1 to Q-421; M-1 to G-420; M-1 to G-419; M-1 to E-418; M-1 to A-417; M-1 to N-416; M-1 to I-415; M-1 to I-414; M-1 to A-413; M-1 to T-412; M-1 to D-411; M-1 to A-410; M-1 to D-409; M-1 to P-408; M-1 to A-407; M-1 to D-406; M-1 to D-405; M-1 to S-404; M-1 to G-403; M-1 to K-402; M-1 to A-401; M-1 to E-400; M-1 to H-399; M-1 to T-398; M-1 to L-397; M-1 to Y-396; M-1 to T-395; M-1 to G-394; M-1 to K-393; M-1 to H-392; M-1 to R-391; M-1 to I-390; M-1 to L-389; M-1 to Y-388; M-1 to H-387; M-1 to G-386; M-1 to L-385; M-1 to F-384; M-1 to I-383; M-1 to L-382; M-1 to M-381; M-1 to I-380; M-1 to L-379; M-1 to L-378; M-1 to L-377; M-1 to F-376; M-1 to V-375; M-1 to I-374; M-1 to F-373; M-1 to A-

372; M-1 to V-371; M-1 to I-370; M-1 to G-369; M-1 to G-368; M-1 to I-367; M-1 to I-366; M-1 to A-365; M-1 to H-364; M-1 to Y-363; M-1 to T-362; M-1 to S-361; M-1 to S-360; M-1 to S-359; M-1 to S-358; M-1 to P-357; M-1 to V-356; M-1 to P-355; M-1 to S-354; M-1 to P-353; M-1 to D-352; M-1 to N-351; M-1 to V-350; M-1 to N-349; M-1 to L-348; M-1 to T-347; M-1 to Y-346; M-1 to Y-345; M-1 to A-344; M-1 to K-343; M-1 to Y-342; M-1 to S-341; M-1 to G-340; M-1 to M-339; M-1 to N-338; M-1 to S-337; M-1 to T-336; M-1 to A-335; M-1 to T-334; M-1 to C-333; M-1 to G-332; M-1 to Y-331; M-1 to T-330; M-1 to G-329; M-1 to S-328; M-1 to D-327; M-1 to S-326; M-1 to K-325; M-1 to N-324; M-1 to L-323; M-1 to F-322; M-1 to P-321; M-1 to F-320; M-1 to I-319; M-1 to L-318; M-1 to A-317; M-1 to S-316; M-1 to E-315; M-1 to Q-314; M-1 to T-313; M-1 to M-312; M-1 to K-311; M-1 to L-310; M-1 to P-309; M-1 to P-308; M-1 to V-307; M-1 to S-306; M-1 to G-305; M-1 to E-304; M-1 to K-303; M-1 to E-302; M-1 to W-301; M-1 to L-300; M-1 to Y-299; M-1 to Q-298; M-1 to Q-297; M-1 to P-296; M-1 to V-295; M-1 to P-294; M-1 to N-293; M-1 to G-292; M-1 to R-291; M-1 to G-290; M-1 to E-289; M-1 to C-288; M-1 to H-287; M-1 to L-286; M-1 to L-285; M-1 to L-284; M-1 to K-283; M-1 to Q-282; M-1 to G-281; M-1 to E-280; M-1 to R-279; M-1 to P-278; M-1 to H-277; M-1 to P-276; M-1 to P-275; M-1 to D-274; M-1 to P-273; M-1 to R-272; M-1 to I-271; M-1 to M-270; M-1 to A-269; M-1 to T-268; M-1 to P-267; M-1 to T-266; M-1 to Y-265; M-1 to L-264; M-1 to V-263; M-1 to E-262; M-1 to I-261; M-1 to R-260; M-1 to Q-259; M-1 to S-258; M-1 to T-257; M-1 to S-256; M-1 to R-255; M-1 to D-254; M-1 to A-253; M-1 to G-252; M-1 to K-251; M-1 to L-250; M-1 to S-249; M-1 to E-248; M-1 to H-247; M-1 to N-246; M-1 to V-245; M-1 to S-244; M-1 to C-243; M-1 to V-242; M-1 to I-241; M-1 to S-240; M-1 to A-239; M-1 to G-238; M-1 to D-237; M-1 to D-236; M-1 to E-235; M-1 to R-234; M-1 to T-233; M-1 to V-232; M-1 to Q-231; M-1 to F-230; M-1 to T-229; M-1 to V-228; M-1 to S-227; M-1 to S-226; M-1 to S-225; M-1 to V-224; M-1 to T-223; M-1 to F-222; M-1 to T-221; M-1 to K-220; M-1 to G-219; M-1 to N-218; M-1 to P-217; M-1 to D-216; M-1 to E-215; M-1 to Q-214; M-1 to I-213; M-1 to R-212; M-1 to T-211; M-1 to P-210; M-1 to E-209; M-1 to G-208; M-1 to H-207; M-1 to L-206; M-1 to E-205; M-1 to Q-204; M-1 to D-203; M-1 to G-202; M-1 to K-201; M-1 to R-200; M-1 to W-199; M-1 to T-198; M-1 to L-197; M-1 to R-196; M-1 to A-195; M-1 to A-194; M-1 to P-193; M-1 to K-192; M-1 to S-191; M-1

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to G-190; M-1 to S-189; M-1 to S-188; M-1 to Q-187; M-1 to C-186; M-1 to N-185; M-1 to L-184; M-1 to T-183; M-1 to A-182; M-1 to T-181; M-1 to D-180; M-1 to K-179; M-1 to E-178; M-1 to R-177; M-1 to L-176; M-1 to S-175; M-1 to S-174; M-1 to K-173; M-1 to Y-172; M-1 to G-171; M-1 to T-170; M-1 to I-169; M-1 to I-168; M-1 to P-167; M-1 to K-166; M-1 to Q-165; M-1 to P-164; M-1 to I-163; M-1 to G-162; M-1 to L-161; M-1 to V-160; M-1 to T-159; M-1 to V-158; M-1 to L-157; M-1 to S-156; M-1 to K-155; M-1 to A-154; M-1 to T-153; M-1 to R-152; M-1 to V-151; M-1 to P-150; M-1 to M-149; M-1 to T-148; M-1 to F-147; M-1 to I-146; M-1 to S-145; M-1 to C-144; M-1 to T-143; M-1 to Y-142; M-1 to E-141; M-1 to G-140; M-1 to E-139; M-1 to D-138; M-1 to A-137; M-1 to L-136; M-1 to A-135; M-1 to V-134; M-1 to N-133; M-1 to S-132; M-1 to I-131; M-1 to S-130; M-1 to I-129; M-1 to S-128; M-1 to L-127; M-1 to E-126; M-1 to H-125; M-1 to P-124; M-1 to T-123; M-1 to S-122; M-1 to T-121; M-1 to V-120; M-1 to L-119; M-1 to Q-118; M-1 to I-117; M-1 to R-116; M-1 to N-115; M-1 to D-114; M-1 to R-113; M-1 to L-112; M-1 to A-111; M-1 to R-110; M-1 to K-109; M-1 to E-108; M-1 to G-107; M-1 to F-106; M-1 to Y-105; M-1 to L-104; M-1 to T-103; M-1 to Q-102; M-1 to Q-101; M-1 to A-100; M-1 to P-99; M-1 to N-98; M-1 to S-97; M-1 to W-96; M-1 to Q-95; M-1 to L-94; M-1 to S-93; M-1 to S-92; M-1 to D-91; M-1 to E-90; M-1 to H-89; M-1 to D-88; M-1 to K-87; M-1 to V-86; M-1 to Q-85; M-1 to C-84; M-1 to K-83; M-1 to L-82; M-1 to V-81; M-1 to V-80; M-1 to T-79; M-1 to G-78; M-1 to G-77; M-1 to A-76; M-1 to V-75; M-1 to V-74; M-1 to T-73; M-1 to E-72; M-1 to D-71; M-1 to S-70; M-1 to T-69; M-1 to W-68; M-1 to P-67; M-1 to Q-66; M-1 to S-65; M-1 to D-64; M-1 to Q-63; M-1 to S-62; M-1 to A-61; M-1 to L-60; M-1 to M-59; M-1 to D-58; M-1 to P-57; M-1 to S-56; M-1 to S-55; M-1 to W-54; M-1 to V-53; M-1 to T-52; M-1 to S-51; M-1 to S-50; M-1 to I-49; M-1 to A-48; M-1 to E-47; M-1 to D-46; M-1 to L-45; M-1 to P-44; M-1 to A-43; M-1 to L-42; M-1 to T-41; M-1 to G-40; M-1 to L-39; M-1 to E-38; M-1 to L-37; M-1 to D-36; M-1 to Q-35; M-1 to E-34; M-1 to Q-33; M-1 to W-32; M-1 to Y-31; M-1 to G-30; M-1 to D-29; M-1 to Q-28; M-1 to S-27; M-1 to L-26; M-1 to N-25; M-1 to A-24; M-1 to G-23; M-1 to G-22; M-1 to P-21; M-1 to A-20; M-1 to W-19; M-1 to C-18; M-1 to C-17; M-1 to A-16; M-1 to F-15; M-1 to L-14; M-1 to L-13; M-1 to L-12; M-1 to L-11; M-1 to L-10; M-1 to L-9; M-1 to L-8; and/or M-1

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to S-7 of SEQ ID NO: 361. Polypeptides encoded by these polynucleotides are also encompassed by the invention.

Also as mentioned above, even if deletion of one or more amino acids from the C-terminus of a protein results in modification of loss of one or more biological functions of the protein (e.g., ability to inhibit the Mixed Lymphocyte Reaction), other functional activities (e.g., biological activities, ability to multimerize, ability to bind ligand, ability to generate antibodies, ability to bind antibodies) may still be retained. For example, the ability of the shortened polypeptide to induce and/or bind to antibodies which recognize the complete or mature forms of the polypeptide generally will be retained when less than the majority of the residues of the complete or mature polypeptide are removed from the C-terminus. Whether a particular polypeptide lacking C-terminal residues of a complete polypeptide retains such immunologic activities can readily be determined by routine methods described herein and otherwise known in the art. It is not unlikely that a polypeptide with a large number of deleted C-terminal amino acid residues may retain some biological or immunogenic activities. In fact, peptides composed of as few as six amino acid residues may often evoke an immune response. Accordingly, the present invention further provides polypeptides having one or more residues deleted from the carboxyl terminus of the amino acid sequence of the polypeptide shown in Figures 3A-3C (SEQ ID NO: 361), as described by the general formula 1-n, where n is an integer from 6 to 432, where n corresponds to the position of the amino acid residue identified in SEQ ID NO: 361.

More in particular, the invention provides polynucleotides encoding polypeptides comprising, or alternatively consisting of, an amino acid sequence selected from the group of N-terminal deletions of the mature extracellular portion of the B7-H4 protein (SEQ ID NO: 1238): L-26 to G-368; S-27 to G-368; Q-28 to G-368; D-29 to G-368; G-30 to G-368; Y-31 to G-368; W-32 to G-368; Q-33 to G-368; E-34 to G-368; Q-35 to G-368; D-36 to G-368; L-37 to G-368; E-38 to G-368; L-39 to G-368; G-40 to G-368; T-41 to G-368; L-42 to G-368; A-43 to G-368; P-44 to G-368; L-45 to G-368; D-46 to G-368; E-47 to G-368; A-48 to G-368; I-49 to G-368; S-50 to G-368; S-51 to G-368; T-52 to G-368; V-53 to G-368; W-54 to G-368; S-55 to G-368; S-56 to G-368; P-57 to G-368; D-58 to G-368; M-59 to G-368; L-60 to G-

368; A-61 to G-368; S-62 to G-368; Q-63 to G-368; D-64 to G-368; S-65 to G-368; Q-66 to G-368; P-67 to G-368; W-68 to G-368; T-69 to G-368; S-70 to G-368; D-71 to G-368; E-72 to G-368; T-73 to G-368; V-74 to G-368; V-75 to G-368; A-76 to G-368; G-77 to G-368; G-78 to G-368; T-79 to G-368; V-80 to G-368; V-81 to G-368; L-82 to G-368; K-83 to G-368; C-84 to G-368; Q-85 to G-368; V-86 to G-368; K-87 to G-368; D-88 to G-368; H-89 to G-368; E-90 to G-368; D-91 to G-368; S-92 to G-368; S-93 to G-368; L-94 to G-368; Q-95 to G-368; W-96 to G-368; S-97 to G-368; N-98 to G-368; P-99 to G-368; A-100 to G-368; Q-101 to G-368; Q-102 to G-368; T-103 to G-368; L-104 to G-368; Y-105 to G-368; F-106 to G-368; G-107 to G-368; E-108 to G-368; K-109 to G-368; R-110 to G-368; A-111 to G-368; L-112 to G-368; R-113 to G-368; D-114 to G-368; N-115 to G-368; R-116 to G-368; I-117 to G-368; Q-118 to G-368; L-119 to G-368; V-120 to G-368; T-121 to G-368; S-122 to G-368; T-123 to G-368; P-124 to G-368; H-125 to G-368; E-126 to G-368; L-127 to G-368; S-128 to G-368; I-129 to G-368; S-130 to G-368; I-131 to G-368; S-132 to G-368; N-133 to G-368; V-134 to G-368; A-135 to G-368; L-136 to G-368; A-137 to G-368; D-138 to G-368; E-139 to G-368; G-140 to G-368; E-141 to G-368; Y-142 to G-368; T-143 to G-368; C-144 to G-368; S-145 to G-368; I-146 to G-368; F-147 to G-368; T-148 to G-368; M-149 to G-368; P-150 to G-368; V-151 to G-368; R-152 to G-368; T-153 to G-368; A-154 to G-368; K-155 to G-368; S-156 to G-368; L-157 to G-368; V-158 to G-368; T-159 to G-368; V-160 to G-368; L-161 to G-368; G-162 to G-368; I-163 to G-368; P-164 to G-368; Q-165 to G-368; K-166 to G-368; P-167 to G-368; I-168 to G-368; I-169 to G-368; T-170 to G-368; G-171 to G-368; Y-172 to G-368; K-173 to G-368; S-174 to G-368; S-175 to G-368; L-176 to G-368; R-177 to G-368; E-178 to G-368; K-179 to G-368; D-180 to G-368; T-181 to G-368; A-182 to G-368; T-183 to G-368; L-184 to G-368; N-185 to G-368; C-186 to G-368; Q-187 to G-368; S-188 to G-368; S-189 to G-368; G-190 to G-368; S-191 to G-368; K-192 to G-368; P-193 to G-368; A-194 to G-368; A-195 to G-368; R-196 to G-368; L-197 to G-368; T-198 to G-368; W-199 to G-368; R-200 to G-368; K-201 to G-368; G-202 to G-368; D-203 to G-368; Q-204 to G-368; E-205 to G-368; L-206 to G-368; H-207 to G-368; G-208 to G-368; E-209 to G-368; P-210 to G-368; T-211 to G-368; R-212 to G-368; I-213 to G-368; Q-214 to G-368; E-215 to G-368; D-216 to G-368; P-217 to G-368; N-218 to G-368; G-219 to G-368; K-220 to G-368; T-221 to G-368; F-222 to G-368;

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T-223 to G-368; V-224 to G-368; S-225 to G-368; S-226 to G-368; S-227 to G-368; V-228 to G-368; T-229 to G-368; F-230 to G-368; Q-231 to G-368; V-232 to G-368; T-233 to G-368; R-234 to G-368; E-235 to G-368; D-236 to G-368; D-237 to G-368; G-238 to G-368; A-239 to G-368; S-240 to G-368; I-241 to G-368; V-242 to G-368; C-243 to G-368; S-244 to G-368; V-245 to G-368; N-246 to G-368; H-247 to G-368; E-248 to G-368; S-249 to G-368; L-250 to G-368; K-251 to G-368; G-252 to G-368; A-253 to G-368; D-254 to G-368; R-255 to G-368; S-256 to G-368; T-257 to G-368; S-258 to G-368; Q-259 to G-368; R-260 to G-368; I-261 to G-368; E-262 to G-368; V-263 to G-368; L-264 to G-368; Y-265 to G-368; T-266 to G-368; P-267 to G-368; T-268 to G-368; A-269 to G-368; M-270 to G-368; I-271 to G-368; R-272 to G-368; P-273 to G-368; D-274 to G-368; P-275 to G-368; P-276 to G-368; H-277 to G-368; P-278 to G-368; R-279 to G-368; E-280 to G-368; G-281 to G-368; Q-282 to G-368; K-283 to G-368; L-284 to G-368; L-285 to G-368; L-286 to G-368; H-287 to G-368; C-288 to G-368; E-289 to G-368; G-290 to G-368; R-291 to G-368; G-292 to G-368; N-293 to G-368; P-294 to G-368; V-295 to G-368; P-296 to G-368; Q-297 to G-368; Q-298 to G-368; Y-299 to G-368; L-300 to G-368; W-301 to G-368; E-302 to G-368; K-303 to G-368; E-304 to G-368; G-305 to G-368; S-306 to G-368; V-307 to G-368; P-308 to G-368; P-309 to G-368; L-310 to G-368; K-311 to G-368; M-312 to G-368; T-313 to G-368; Q-314 to G-368; E-315 to G-368; S-316 to G-368; A-317 to G-368; L-318 to G-368; I-319 to G-368; F-320 to G-368; P-321 to G-368; F-322 to G-368; L-323 to G-368; N-324 to G-368; K-325 to G-368; S-326 to G-368; D-327 to G-368; S-328 to G-368; G-329 to G-368; T-330 to G-368; Y-331 to G-368; G-332 to G-368; C-333 to G-368; T-334 to G-368; A-335 to G-368; T-336 to G-368; S-337 to G-368; N-338 to G-368; M-339 to G-368; G-340 to G-368; S-341 to G-368; Y-342 to G-368; K-343 to G-368; A-344 to G-368; Y-345 to G-368; Y-346 to G-368; T-347 to G-368; L-348 to G-368; N-349 to G-368; V-350 to G-368; N-351 to G-368; D-352 to G-368; P-353 to G-368; S-354 to G-368; P-355 to G-368; V-356 to G-368; P-357 to G-368; S-358 to G-368; S-359 to G-368; S-360 to G-368; S-361 to G-368; T-362 to G-368; and/or Y-363 to G-368 of SEQ ID NO: 1238. Polypeptides encoded by these polynucleotides are also encompassed by the invention.

Additionally, the invention provides polynucleotides encoding polypeptides comprising, or alternatively consisting of, an amino acid sequence selected from the

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group of C-terminal deletions of the mature extracellular portion of the B7-H4 protein (SEQ ID NO: 1238): N-25 to I-367; N-25 to I-366; N-25 to A-365; N-25 to H-364; N-25 to Y-363; N-25 to T-362; N-25 to S-361; N-25 to S-360; N-25 to S-359; N-25 to S-358; N-25 to P-357; N-25 to V-356; N-25 to P-355; N-25 to S-354; N-25 to P-353; N-25 to D-352; N-25 to N-351; N-25 to V-350; N-25 to N-349; N-25 to L-348; N-25 to T-347; N-25 to Y-346; N-25 to Y-345; N-25 to A-344; N-25 to K-343; N-25 to Y-342; N-25 to S-341; N-25 to G-340; N-25 to M-339; N-25 to N-338; N-25 to S-337; N-25 to T-336; N-25 to A-335; N-25 to T-334; N-25 to C-333; N-25 to G-332; N-25 to Y-331; N-25 to T-330; N-25 to G-329; N-25 to S-328; N-25 to D-327; N-25 to S-326; N-25 to K-325; N-25 to N-324; N-25 to L-323; N-25 to F-322; N-25 to P-321; N-25 to F-320; N-25 to I-319; N-25 to L-318; N-25 to A-317; N-25 to S-316; N-25 to E-315; N-25 to Q-314; N-25 to T-313; N-25 to M-312; N-25 to K-311; N-25 to L-310; N-25 to P-309; N-25 to P-308; N-25 to V-307; N-25 to S-306; N-25 to G-305; N-25 to E-304; N-25 to K-303; N-25 to E-302; N-25 to W-301; N-25 to L-300; N-25 to Y-299; N-25 to Q-298; N-25 to Q-297; N-25 to P-296; N-25 to V-295; N-25 to P-294; N-25 to N-293; N-25 to G-292; N-25 to R-291; N-25 to G-290; N-25 to E-289; N-25 to C-288; N-25 to H-287; N-25 to L-286; N-25 to L-285; N-25 to L-284; N-25 to K-283; N-25 to Q-282; N-25 to G-281; N-25 to E-280; N-25 to R-279; N-25 to P-278; N-25 to H-277; N-25 to P-276; N-25 to P-275; N-25 to D-274; N-25 to P-273; N-25 to R-272; N-25 to I-271; N-25 to M-270; N-25 to A-269; N-25 to T-268; N-25 to P-267; N-25 to T-266; N-25 to Y-265; N-25 to L-264; N-25 to V-263; N-25 to E-262; N-25 to I-261; N-25 to R-260; N-25 to Q-259; N-25 to S-258; N-25 to T-257; N-25 to S-256; N-25 to R-255; N-25 to D-254; N-25 to A-253; N-25 to G-252; N-25 to K-251; N-25 to L-250; N-25 to S-249; N-25 to E-248; N-25 to H-247; N-25 to N-246; N-25 to V-245; N-25 to S-244; N-25 to C-243; N-25 to V-242; N-25 to I-241; N-25 to S-240; N-25 to A-239; N-25 to G-238; N-25 to D-237; N-25 to D-236; N-25 to E-235; N-25 to R-234; N-25 to T-233; N-25 to V-232; N-25 to Q-231; N-25 to F-230; N-25 to T-229; N-25 to V-228; N-25 to S-227; N-25 to S-226; N-25 to S-225; N-25 to V-224; N-25 to T-223; N-25 to F-222; N-25 to T-221; N-25 to K-220; N-25 to G-219; N-25 to N-218; N-25 to P-217; N-25 to D-216; N-25 to E-215; N-25 to Q-214; N-25 to I-213; N-25 to R-212; N-25 to T-211; N-25 to P-210; N-25 to E-209; N-25 to G-208; N-25 to H-207; N-25 to L-206; N-25 to E-205; N-25 to Q-204; N-25 to D-203;

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N-25 to G-202; N-25 to K-201; N-25 to R-200; N-25 to W-199; N-25 to T-198; N-25 to L-197; N-25 to R-196; N-25 to A-195; N-25 to A-194; N-25 to P-193; N-25 to K-192; N-25 to S-191; N-25 to G-190; N-25 to S-189; N-25 to S-188; N-25 to Q-187; N-25 to C-186; N-25 to N-185; N-25 to L-184; N-25 to T-183; N-25 to A-182; N-25 to T-181; N-25 to D-180; N-25 to K-179; N-25 to E-178; N-25 to R-177; N-25 to L-176; N-25 to S-175; N-25 to S-174; N-25 to K-173; N-25 to Y-172; N-25 to G-171; N-25 to T-170; N-25 to I-169; N-25 to I-168; N-25 to P-167; N-25 to K-166; N-25 to Q-165; N-25 to P-164; N-25 to I-163; N-25 to G-162; N-25 to L-161; N-25 to V-160; N-25 to T-159; N-25 to V-158; N-25 to L-157; N-25 to S-156; N-25 to K-155; N-25 to A-154; N-25 to T-153; N-25 to R-152; N-25 to V-151; N-25 to P-150; N-25 to M-149; N-25 to T-148; N-25 to F-147; N-25 to I-146; N-25 to S-145; N-25 to C-144; N-25 to T-143; N-25 to Y-142; N-25 to E-141; N-25 to G-140; N-25 to E-139; N-25 to D-138; N-25 to A-137; N-25 to L-136; N-25 to A-135; N-25 to V-134; N-25 to N-133; N-25 to S-132; N-25 to I-131; N-25 to S-130; N-25 to I-129; N-25 to S-128; N-25 to L-127; N-25 to E-126; N-25 to H-125; N-25 to P-124; N-25 to T-123; N-25 to S-122; N-25 to T-121; N-25 to V-120; N-25 to L-119; N-25 to Q-118; N-25 to I-117; N-25 to R-116; N-25 to N-115; N-25 to D-114; N-25 to R-113; N-25 to L-112; N-25 to A-111; N-25 to R-110; N-25 to K-109; N-25 to E-108; N-25 to G-107; N-25 to F-106; N-25 to Y-105; N-25 to L-104; N-25 to T-103; N-25 to Q-102; N-25 to Q-101; N-25 to A-100; N-25 to P-99; N-25 to N-98; N-25 to S-97; N-25 to W-96; N-25 to Q-95; N-25 to L-94; N-25 to S-93; N-25 to S-92; N-25 to D-91; N-25 to E-90; N-25 to H-89; N-25 to D-88; N-25 to K-87; N-25 to V-86; N-25 to Q-85; N-25 to C-84; N-25 to K-83; N-25 to L-82; N-25 to V-81; N-25 to V-80; N-25 to T-79; N-25 to G-78; N-25 to G-77; N-25 to A-76; N-25 to V-75; N-25 to V-74; N-25 to T-73; N-25 to E-72; N-25 to D-71; N-25 to S-70; N-25 to T-69; N-25 to W-68; N-25 to P-67; N-25 to Q-66; N-25 to S-65; N-25 to D-64; N-25 to Q-63; N-25 to S-62; N-25 to A-61; N-25 to L-60; N-25 to M-59; N-25 to D-58; N-25 to P-57; N-25 to S-56; N-25 to S-55; N-25 to W-54; N-25 to V-53; N-25 to T-52; N-25 to S-51; N-25 to S-50; N-25 to I-49; N-25 to A-48; N-25 to E-47; N-25 to D-46; N-25 to L-45; N-25 to P-44; N-25 to A-43; N-25 to L-42; N-25 to T-41; N-25 to G-40; N-25 to L-39; N-25 to E-38; N-25 to L-37; N-25 to D-36; N-25 to Q-35; N-25 to E-34; N-25 to Q-33; N-25 to W-32; and/or

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N-25 to Y-31 of SEQ ID NO: 1238. Polypeptides encoded by these polynucleotides are also encompassed by the invention.

In addition, any of the above listed N- or C-terminal deletions can be combined to produce a N- and C-terminal deleted polypeptide. The invention also provides polypeptides comprising, or alternatively consisting of, one or more amino acids deleted from both the amino and the carboxyl termini, which may be described generally as having residues m-n of SEQ ID NO: 361, where n and m are integers as described above. Polynucleotides encoding these polypeptides are also encompassed by the invention.

The present invention is also directed to proteins containing polypeptides at least 80%, 85%, 90%, 92%, 93%, 94%, 95%, 96%, 97%, 98% or 99% identical to a polypeptide sequence set forth herein as m-n. In preferred embodiments, the application is directed to proteins containing polypeptides at least 80%, 85%, 90%, 95%, 96%, 97%, 98% or 99% identical to polypeptides having the amino acid sequence of the specific N- and C-terminal deletions recited herein. Polynucleotides encoding these polypeptides are also encompassed by the invention.

Also included are polynucleotide sequences encoding a polypeptide consisting of a portion of the complete amino acid sequence encoded by a cDNA clone contained in ATCC Deposit Nos. 209007 (deposited on April 28, 1997) and 209083 (deposited on May 29, 1997), where this portion excludes any integer of amino acid residues from 1 to about 228 amino acids from the amino terminus of the complete amino acid sequence encoded by a cDNA clone contained in ATCC Deposit Nos. 209007 and 209083, or any integer of amino acid residues from 1 to about 228 amino acids from the carboxyl terminus, or any combination of the above amino terminal and carboxyl terminal deletions, of the complete amino acid sequence encoded by the cDNA clone contained in ATCC Deposit Nos. 209007 and 209083. Polypeptides encoded by these polynucleotides also are encompassed by the invention.

As described herein or otherwise known in the art, the polynucleotides of the invention have uses that include, but are not limited to, serving as probes or primers in chromosome identification, chromosome mapping, and linkage analysis.

Polynucleotides and polypeptides of the invention are useful as reagents for differential identification of CNS and/or immune system tissue(s) or cell type(s)

present in a biological sample and for diagnosis of diseases and conditions which include, but are not limited to, diseases and/or disorders involving immune system activation, stimulation and/or surveillance, particularly involving T cells and/or neutrophils, susceptibility to viral disease and diseases of the CNS, especially cancers of that system. Similarly, polypeptides and antibodies directed to these polypeptides are useful in providing immunological probes for differential identification of the tissue(s) or cell type(s). Particularly contemplated are the use of antibodies directed against the extracellular portion of this protein which act as antagonists and/or agonists for the activity of the B7-H4 protein. Such antagonistic/agonist antibodies would be useful for the prevention and/or inhibition of such biological activities as are disclosed herein (e.g., T cell modulated activities).

For a number of disorders of the above tissues or cells, particularly of the immune system and CNS, expression of this gene at significantly higher or lower levels may be routinely detected in certain tissues or cell types (e.g., immune, CNS, cancerous and wounded tissues) or bodily fluids (e.g., lymph, serum, plasma, urine, synovial fluid and spinal fluid) or another tissue or cell sample taken from an individual having such a disorder, relative to the standard gene expression level, i.e., the expression level in healthy tissue or bodily fluid from an individual not having the disorder.

The homology to members of the B7 family of ligands indicates that the polynucleotides and polypeptides corresponding to this gene are useful for the diagnosis, detection and/or treatment of diseases and/or disorders involving immune system activation, stimulation and/or surveillance, particularly as relating to T cells and/or neutrophils. In particular, the translation product of the B7-H4 gene may be involved in the costimulation of T cells, binding to ICOS, and/or may play a role in modulation of the expression of particular cytokines.

More generally, this gene product may be involved in the regulation of cytokine production, antigen presentation, or other processes that may also suggest a usefulness in the treatment of cancer (e.g., by boosting immune responses). Since the gene is expressed in cells of lymphoid origin, the gene or protein, as well as, antibodies directed against the protein may show utility as a tumor marker and/or immunotherapy targets for the above listed tissues. Therefore it may be also used as

an agent for immunological disorders including arthritis, asthma, immune deficiency diseases such as AIDS, leukemia, rheumatoid arthritis, inflammatory bowel disease, sepsis, acne, and psoriasis. In addition, this gene product may have commercial utility in the expansion of stem cells and committed progenitors of various blood lineages, and in the differentiation and/or proliferation of various cell types. Furthermore, the protein may also be used to determine biological activity, to raise antibodies, as tissue markers, to isolate cognate ligands or receptors, to identify agents that modulate their interactions, in addition to its use as a nutritional supplement.

The tissue distribution and homology to poliovirus receptor precursors suggests that the protein product of this clone would be useful for the treatment and prevention of diseases that involve the binding and uptake of virus particles for infection. It might also be helpful in genetic therapy where the goal is to insert foreign DNA into infected cells. With the help of this protein, the binding and uptake of this foreign DNA might be aided. In addition, it is expected that over expression of this gene will indicate abnormalities involving the CNS, particularly cancers of that system. Protein, as well as, antibodies directed against the protein may show utility as a tumor marker and/or immunotherapy targets for the above listed tissues.

Many polynucleotide sequences, such as EST sequences, are publicly available and accessible through sequence databases. Some of these sequences are related to SEQ ID NO: 123 and may have been publicly available prior to conception of the present invention. Preferably, such related polynucleotides are specifically excluded from the scope of the present invention. To list every related sequence would be cumbersome. Accordingly, preferably excluded from the present invention are one or more polynucleotides comprising a nucleotide sequence described by the general formula of a-b, where a is any integer between 1 to 2523 of SEQ ID NO: 123, b is an integer of 15 to 2537, where both a and b correspond to the positions of nucleotide residues shown in SEQ ID NO: 123

FEATURES OF PROTEIN ENCODED BY GENE NO: 114

The translation product of this gene shares sequence homology with YO87_CAEEL hypothetical 28.5 KD protein ZK1236.7 in chromosome III of Caenorhabditis elegans in addition to alpha-1 collagen type III (See Genbank Accession No. gi|537432). In specific embodiments, polypeptides of the invention comprise, or alternatively consists of, an amino acid sequence selected from the group: VPELPDRVHQLHQAVQGCALGRPGFPGGPTHSGHHKSHPGPAGGDYNRCDR PGQVHLHNPRGTGRRGQLHPTAGPGVHRRACPSQQLPHRLGPGVPCPSPSLT PVLPSWTQSWCGLPGYTSSS (SEQ ID NO:954), VHQLHQAVQGCALGRPGFPGGP (SEQ ID NO:955), PTHSGHHKSHPGPAGGDYNRCDRPGQVHLHNPRGTGRRGQLH (SEQ ID NO:956), and/or LHPTAGPGVHRRACPSQQLPHRLGPGVPCPSPSLTPVLPSWTQSWCGLPGYTS SS (SEQ ID NO:957). Moreover, fragments and variants of these polypeptides (such as, for example, fragments as described herein, polypeptides at least 80%, 85%, 90%, 95%, 96%, 97%, 98%, or 99% identical to these polypeptides and polypeptides encoded by the polynucleotide which hybridizes, under stringent conditions, to the polynucleotide encoding these polypeptides) are encompassed by the invention. Antibodies that bind polypeptides of the invention are also encompassed by the invention. Polynucleotides encoding these polypeptides are also encompassed by the invention.

This gene is expressed primarily in brain cells, and to a lesser extent in activated B and T cells.

Polynucleotides and polypeptides of the invention are useful as reagents for differential identification of the tissue(s) or cell type(s) present in a biological sample and for diagnosis of diseases and conditions which include, but are not limited to, neurodegeneration and immunological disorders. Similarly, polypeptides and antibodies directed to these polypeptides are useful in providing immunological probes for differential identification of the tissue(s) or cell type(s). For a number of disorders of the above tissues or cells, particularly of the neural and immune systems, expression of this gene at significantly higher or lower levels may be routinely detected in certain tissues or cell types (e.g. brain, immune, cancerous and wounded tissues) or bodily fluids (e.g., lymph, serum, plasma, urine, synovial fluid and spinal

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fluid) or another tissue or cell sample taken from an individual having such a disorder, relative to the standard gene expression level, i.e., the expression level in healthy tissue or bodily fluid from an individual not having the disorder.

Predicted epitopes include those comprising a sequence shown in SEQ ID NO: 362 as residues: Glu-34 to Glu-39, Gly-51 to Ser-72, Ala-88 to Glu-93, Gln-100 to Val-105.

The tissue distribution in brain cells, combined with the homology to YO87_CAEEL hypothetical 28.5 KD protein ZK1236.7 in chromosome III of Caenorhabditis elegans as well as to a conserved alpha-1 collagen type III protein indicates that the protein product of this gene is useful for the detection and treatment of neurodegenerative disease states and behavioral disorders such as Alzheimer's Disease, Parkinson's Disease, Huntington's Disease, schizophrenia, mania, dementia, paranoia, obsessive compulsive disorder and panic disorders. Because the gene is expressed in cells of lymphoid origin, the natural gene product may be involved in immune functions. Therefore it may be also used as an agent for immunological disorders including arthritis, asthma, immune deficiency diseases such as AIDS, and leukemia. Protein, as well as, antibodies directed against the protein may show utility as a tissue-specific marker and/or immunotherapy target for the above listed tissues.

Many polynucleotide sequences, such as EST sequences, are publicly available and accessible through sequence databases. Some of these sequences are related to SEQ ID NO:124 and may have been publicly available prior to conception of the present invention. Preferably, such related polynucleotides are specifically excluded from the scope of the present invention. To list every related sequence is cumbersome. Accordingly, preferably excluded from the present invention are one or more polynucleotides comprising a nucleotide sequence described by the general formula of a-b, where a is any integer between 1 to 1376 of SEQ ID NO:124, b is an integer of 15 to 1390, where both a and b correspond to the positions of nucleotide residues shown in SEQ ID NO:124, and where b is greater than or equal to a + 14.

FEATURES OF PROTEIN ENCODED BY GENE NO: 115

Docket No. 2000.07.00

The translation product of this gene shares sequence homology with alpha 3 type IX collagen, which is thought to be important in hyaline cartilage formation via its ability to uptake inorganic sulfate by cells (See Genbank Accession No. gi|975657).

In specific embodiments, polypeptides of the invention comprise, or alternatively consists of, an amino acid sequence selected from the group: SLRRPRSAAXQTLTTFLSSVSSASSSALPGSREPCDPRAPPPPRSGSAASCCSCC CSCPRRRAPLRSPRGSKRRIRQREVVDLYNGMCLQGPAGVPGRDGSPGANGI PGTPGIPGRDGFKGEKGECLRESFEESWTPNYKQCSWSSLNYGIDLGKIAECT FTKMRSNSALRVLFSGSLRLKCRNACCQRWYFTFNGAECSGPLPIEAIIYLDQ GSPEMNSTINIHRTSSVEGLCEGIGAGLVDVAIWVGTCSDYPKGDASTGWNS VSRIIIEELPK(SEQ ID NO:958), SLRRPRSAAXQTLTTFLSSVSSASSSALPGSREPCDPRAPPPPRSGSAASCCSCC CSCPRR (SEQ ID NO:959), RAPLRSPRGSKRRIRQREVVDLYNGMCLQGPAGVPGRDGSPGANGIPGTPGI (SEQ ID NO:960), TPGIPGRDGFKGEKGECLRESFEESWTPNYKQCSWSSLNYGIDLGKIAECTF (SEQ ID NO:961), FTKMRSNSALRVLFSGSLRLKCRNACCQRWYFTFNGAECSGPLPIEAIIYLDQ GSPEMNSTINIHR (SEQ ID NO:962), and/or RTSSVEGLCEGIGAGLVDVAIWVGTCSDYPKGDASTGWNSVSRIIIEELPK (SEQ ID NO:963). Moreover, fragments and variants of these polypeptides (such as, for example, fragments as described herein, polypeptides at least 80%, 85%, 90%, 95%, 96%, 97%, 98%, or 99% identical to these polypeptides and polypeptides encoded by the polynucleotide which hybridizes, under stringent conditions, to the polynucleotide encoding these polypeptides) are encompassed by the invention. Antibodies that bind polypeptides of the invention are also encompassed by the invention. Polynucleotides encoding these polypeptides are also encompassed by the invention.

This gene is expressed primarily in smooth muscle, and to a lesser extent in synovial tissue.

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Polynucleotides and polypeptides of the invention are useful as reagents for differential identification of the tissue(s) or cell type(s) present in a biological sample and for diagnosis of diseases and conditions which include, but are not limited to, dwarfism, spinal deformation, and specific joint abnormalities as well as chondrodysplasias, i.e. spondyloepiphyseal dysplasia congenita, familial osteoarthritis, Atelosteogenesis type II, metaphyseal chondrodysplasia type Schmid and autoimmune disorders . Similarly, polypeptides and antibodies directed to these polypeptides are useful in providing immunological probes for differential identification of the tissue(s) or cell type(s). For a number of disorders of the above tissues or cells, particularly of the skeletal system, expression of this gene at significantly higher or lower levels may be routinely detected in certain tissues or cell types (e.g. muscle, synovial tissues, cancerous and wounded tissues) or bodily fluids (e.g., lymph, serum, plasma, urine, synovial fluid and spinal fluid) or another tissue or cell sample taken from an individual having such a disorder, relative to the standard gene expression level, i.e., the expression level in healthy tissue or bodily fluid from an individual not having the disorder.

The tissue distribution in smooth muscle, and homology to alpha 3 type IX collagen indicates that the protein product of this gene is useful for the treatment and diagnosis of diseases associated with the mutation in this gene which leads to the many different types of chondrodysplasias. By the use of this product, the abnormal growth and development of bones of the limbs and spine could be detected or treated *in utero*, since the protein or polypeptides thereof could affect epithelial cells early in development, and later the chondrocytes of the developing craniofacial structure. In addition, the expression of this gene product in synovium would suggest a role in the detection and treatment of disorders and conditions affecting the skeletal system, in particular osteoporosis as well as disorders afflicting connective tissues (e.g. arthritis, trauma, tendonitis, chrondomalacia and inflammation), such as in the diagnosis or treatment of various autoimmune disorders such as rheumatoid arthritis, lupus, scleroderma, and dermatomyositis as well as dwarfism, spinal deformation, and specific joint abnormalities as well as chondrodysplasias (i.e. spondyloepiphyseal dysplasia congenita, familial osteoarthritis, Atelosteogenesis type II, metaphyseal chondrodysplasia type Schmid). Moreover, the expression within smooth muscle

indicates t that polynucleotides and polypeptides corresponding to this gene are useful for the treatment, detection, and/or prevention of a variety of vascular disorders, which include, but are not limited to, atherosclerosis, embolism, stroke, aneurysm, or microvascular disease. Protein, as well as, antibodies directed against the protein may show utility as a tumor marker and/or immunotherapy targets for the above listed tissues.

Many polynucleotide sequences, such as EST sequences, are publicly available and accessible through sequence databases. Some of these sequences are related to SEQ ID NO:125 and may have been publicly available prior to conception of the present invention. Preferably, such related polynucleotides are specifically excluded from the scope of the present invention. To list every related sequence is cumbersome. Accordingly, preferably excluded from the present invention are one or more polynucleotides comprising a nucleotide sequence described by the general formula of a-b, where a is any integer between 1 to 1274 of SEQ ID NO:125, b is an integer of 15 to 1288, where both a and b correspond to the positions of nucleotide residues shown in SEQ ID NO:125, and where b is greater than or equal to a + 14.

DOCUMENT #: 6000000

FEATURES OF PROTEIN ENCODED BY GENE NO: 116

The translation product of this gene shares sequence homology with retrovirus-related reverse transcriptase, which is thought to be important in viral replication.

In specific embodiments, polypeptides of the invention comprise, or alternatively consists of, the following amino acid sequence: TKKENCRPASLMNIDTKILNKILMNQ (SEQ ID NO:964). Moreover, fragments and variants of this polypeptide (such as, for example, fragments as described herein, polypeptides at least 80%, 85%, 90%, 95%, 96%, 97%, 98%, or 99% identical to these polypeptides and polypeptides encoded by the polynucleotide which hybridize, under stringent conditions, to the polynucleotide encoding this polypeptide are encompassed by the invention. Antibodies that bind polypeptides of the invention are also encompassed by the invention. Polynucleotides encoding this polypeptide are

also encompassed by the invention. (See Genbank Accession No. pir|A25313|GNHUL1).

This gene is expressed primarily in human meningima.

Polynucleotides and polypeptides of the invention are useful as reagents for differential identification of the tissue(s) or cell type(s) present in a biological sample and for diagnosis of diseases and conditions which include, but are not limited to, retroviral diseases such as AIDS, and possibly certain cancers due to transactivation of latent cell division genes. Similarly, polypeptides and antibodies directed to these polypeptides are useful in providing immunological probes for differential identification of the tissue(s) or cell type(s). For a number of disorders of the above tissues or cells, particularly of the immune system, expression of this gene at significantly higher or lower levels may be routinely detected in certain tissues or cell types (e.g. meningima, cancerous and wounded tissues) or bodily fluids (e.g., lymph, serum, plasma, urine, synovial fluid and spinal fluid) or another tissue or cell sample taken from an individual having such a disorder, relative to the standard gene expression level, i.e., the expression level in healthy tissue or bodily fluid from an individual not having the disorder.

The tissue distribution in human meningima, combined with the homology to a retrovirus-related reverse transcriptase indicates that the protein product of this gene is useful for the detection and treatment of diseases and conditions associated with retroviral infection, since a functional reverse transcriptase (RT) or RT-like molecule is an integral component of the retroviral life cycle. Protein, as well as, antibodies directed against the protein may show utility as a tumor marker and/or immunotherapy targets for the above listed tissues.

Many polynucleotide sequences, such as EST sequences, are publicly available and accessible through sequence databases. Some of these sequences are related to SEQ ID NO:126 and may have been publicly available prior to conception of the present invention. Preferably, such related polynucleotides are specifically excluded from the scope of the present invention. To list every related sequence is cumbersome. Accordingly, preferably excluded from the present invention are one or more polynucleotides comprising a nucleotide sequence described by the general formula of a-b, where a is any integer between 1 to 1503 of SEQ ID NO:126, b is an

integer of 15 to 1517, where both a and b correspond to the positions of nucleotide residues shown in SEQ ID NO:126, and where b is greater than or equal to a + 14.

FEATURES OF PROTEIN ENCODED BY GENE NO: 117

The translation product of this gene shares sequence homology with an unknown gene from C. elegans, as well as weak homolog with mammalian metaxin, a gene contiguous to both thrombospondin 3 and glucocerebrosidase, and is known to be required for embryonic development. Recently another group cloned and sequenced this gene from humans, naming it metaxin 2. It is thought that metaxin 1 and metaxin 2 interact, and are associated with the mammalian mitochondrial outer membrane (See Genbank Accession No. AF053551).

In specific embodiments, polypeptides of the invention comprise, or alternatively consists of, an amino acid sequence selected from the group: MCNLPIKVVCRANAEYMSPSGKVPXXHVGNQVVSELGPIVQFVKAKGHSLS DGLEEVQKAEMKAYMELVNNMLLTAELYLQWCDEATVGXITHXRYGSPYP WPLXHILAYQKQWEVKRKXKAIGWGKKTLDQVLEDVDQCCQALSQRLGTQ PYFFNKQPTELDALVFGHLYTILTTQLTNDELSEKVKNYSNLLAFCRRIEQHY FED RGKGRLS (SEQ ID NO:965), MCNLPIKVVCRANAEYMSPSGKVPXXHVGNQVVSELGPIVQFVK (SEQ ID NO:966), FVKAKGHSLSDGLEEVQKAEMKAYMELVNNMLLTAELYLQWCDE (SEQ ID NO:967), LQWCDEATVGXITHXRYGSPYPWP LXHILAYQKQWEVKRKXKAIGWGKKTL (SEQ ID NO:968), DQVLEDVDQCCQ ALSQRLGTQPYFFNKQPTELDALVFGHLYTI (SEQ ID NO:969), and/or LTTQLTNDELSEKVKNYSNLLAFCRRIEQHYFEDRGKGRLS (SEQ ID NO:970). Moreover, fragments and variants of these polypeptides (such as, for example, fragments as described herein, polypeptides at least 80%, 85%, 90%, 95%, 96%, 97%, 98%, or 99% identical to these polypeptides and polypeptides encoded by the polynucleotide which hybridizes, under stringent conditions, to the polynucleotide encoding these polypeptides) are encompassed by the invention. Antibodies that bind polypeptides of the invention are also encompassed by the

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invention. Polynucleotides encoding these polypeptides are also encompassed by the invention. (See Genbank Accession No. gi|1326108).

The gene encoding the disclosed cDNA is thought to reside on chromosome 2. Accordingly, polynucleotides related to this invention are useful as a marker in linkage analysis for chromosome 2.

This gene is expressed primarily in fetal tissues, and to a lesser extent in hematopoietic cells and tissues, including spleen, monocytes, and T cells.

Polynucleotides and polypeptides of the invention are useful as reagents for differential identification of the tissue(s) or cell type(s) present in a biological sample and for diagnosis of diseases and conditions which include, but are not limited to, cancer; lymphoproliferative disorders; inflammation; chondrosarcoma, and Gaucher disease. Similarly, polypeptides and antibodies directed to these polypeptides are useful in providing immunological probes for differential identification of the tissue(s) or cell type(s). For a number of disorders of the above tissues or cells, particularly of the hematopoietic and embryonic systems, expression of this gene at significantly higher or lower levels may be routinely detected in certain tissues or cell types (e.g. immune, fetal, cancerous and wounded tissues) or bodily fluids (e.g., lymph, serum, plasma, urine, synovial fluid and spinal fluid) or another tissue or cell sample taken from an individual having such a disorder, relative to the standard gene expression level, i.e., the expression level in healthy tissue or bodily fluid from an individual not having the disorder.

The tissue distribution in fetal tissues indicates that the protein product of this gene is useful for the diagnosis and treatment of cancer and other proliferative disorders. Moreover, this protein may play a role in the regulation of cellular division. Additionally, the expression in hematopoietic cells and tissues indicates that this protein may play a role in the proliferation, differentiation, and survival of hematopoietic cell lineages. Thus, this gene may be useful in the treatment of lymphoproliferative disorders, and in the maintenance and differentiation of various hematopoietic lineages from early hematopoietic stem and committed progenitor cells. Protein, as well as, antibodies directed against the protein may show utility as a tumor marker and/or immunotherapy targets for the above listed tissues.

Many polynucleotide sequences, such as EST sequences, are publicly available and accessible through sequence databases. Some of these sequences are related to SEQ ID NO:127 and may have been publicly available prior to conception of the present invention. Preferably, such related polynucleotides are specifically excluded from the scope of the present invention. To list every related sequence is cumbersome. Accordingly, preferably excluded from the present invention are one or more polynucleotides comprising a nucleotide sequence described by the general formula of a-b, where a is any integer between 1 to 1059 of SEQ ID NO:127, b is an integer of 15 to 1073, where both a and b correspond to the positions of nucleotide residues shown in SEQ ID NO:127, and where b is greater than or equal to a + 14.

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FEATURES OF PROTEIN ENCODED BY GENE NO: 118

The translation product of this gene shares sequence homology with reverse transcriptase, which is important in the synthesis of a cDNA chain from an RNA molecule, and is a method whereby the infecting RNA chains of retroviruses are transcribed into their DNA complements.

In specific embodiments, polypeptides of the invention comprise, or alternatively consists of, an amino acid sequence selected from the group: MXXXNSHITIFTLNVNGLNAPNERHRLANWIQSQDQVCCIQETHLTGRDTHR LKIKGWRKIYQANGKQKK (SEQ ID NO:971), FTLNVNGLNAPNERHRLANWIQSQDQVC (SEQ ID NO:972), THLTGRDTHRLKIKGWR (SEQ ID NO:973), and/or GWRKIYQANGKQKK (SEQ ID NO:974). Moreover, fragments and variants of these polypeptides (such as, for example, fragments as described herein, polypeptides at least 80%, 85%, 90%, 95%, 96%, 97%, 98%, or 99% identical to these polypeptides and polypeptides encoded by the polynucleotide which hybridizes, under stringent conditions, to the polynucleotide encoding these polypeptides) are encompassed by the invention. Antibodies that bind polypeptides of the invention are also encompassed by the invention. Polynucleotides encoding these polypeptides are also encompassed by the invention. (See Genbank Accession No. gi|2072964).

This gene is expressed primarily in skin, and to a lesser extent in neutrophils.

Polynucleotides and polypeptides of the invention are useful as reagents for differential identification of the tissue(s) or cell type(s) present in a biological sample and for diagnosis of diseases and conditions which include, but are not limited to, cancers; hematopoietic disorders; inflammation; disorders of immune surveillance. Similarly, polypeptides and antibodies directed to these polypeptides are useful in providing immunological probes for differential identification of the tissue(s) or cell type(s). For a number of disorders of the above tissues or cells, particularly of the epidermis and/or hematopoietic system, expression of this gene at significantly higher or lower levels may be routinely detected in certain tissues or cell types (e.g. skin, immune, cancerous and wounded tissues) or bodily fluids (e.g., lymph, serum, plasma, urine, synovial fluid and spinal fluid) or another tissue or cell sample taken from an individual having such a disorder, relative to the standard gene expression level, i.e., the expression level in healthy tissue or bodily fluid from an individual not having the disorder.

The tissue distribution in skin, combined with the homology to a reverse transcriptase indicates that the protein product of this gene is useful for cancer therapy, particularly of the integumentary system. Expression in the skin also indicates that this gene is useful in wound healing and fibrosis. Expression by neutrophils also indicates that this gene product plays a role in inflammation and the control of immune surveillance (i.e., recognition of viral pathogens). Reverse transcriptase family members are also useful in the detection and treatment of AIDS. Protein, as well as, antibodies directed against the protein may show utility as a tumor marker and/or immunotherapy targets for the above listed tissues.

Many polynucleotide sequences, such as EST sequences, are publicly available and accessible through sequence databases. Some of these sequences are related to SEQ ID NO:128 and may have been publicly available prior to conception of the present invention. Preferably, such related polynucleotides are specifically excluded from the scope of the present invention. To list every related sequence is cumbersome. Accordingly, preferably excluded from the present invention are one or more polynucleotides comprising a nucleotide sequence described by the general formula of a-b, where a is any integer between 1 to 286 of SEQ ID NO:128, b is an

integer of 15 to 300, where both a and b correspond to the positions of nucleotide residues shown in SEQ ID NO:128, and where b is greater than or equal to a + 14.

FEATURES OF PROTEIN ENCODED BY GENE NO: 119

The translation product of this gene shares sequence homology with reverse transcriptase, which is important in the synthesis of a cDNA copy of an RNA molecule, and is a method whereby a retrovirus reverse-transcribes its genome into an inheritable DNA copy.

This gene is expressed primarily in the frontal cortex of brain.

Polynucleotides and polypeptides of the invention are useful as reagents for differential identification of the tissue(s) or cell type(s) present in a biological sample and for diagnosis of diseases and conditions which include, but are not limited to, cancer and neurodegenerative disorders. Similarly, polypeptides and antibodies directed to these polypeptides are useful in providing immunological probes for differential identification of the tissue(s) or cell type(s). For a number of disorders of the above tissues or cells, particularly of the CNS and peripheral nervous system, expression of this gene at significantly higher or lower levels may be routinely detected in certain tissues or cell types (e.g. brain, cancerous and wounded tissues) or bodily fluids (e.g., lymph, serum, plasma, urine, synovial fluid and spinal fluid) or another tissue or cell sample taken from an individual having such a disorder, relative to the standard gene expression level, i.e., the expression level in healthy tissue or bodily fluid from an individual not having the disorder.

The tissue distribution in the frontal cortex, combined with the homology to a reverse transcriptase suggest that this gene is useful in the treatment of cancer and AIDS, particularly of the neural system. The expression in brain indicates that it plays a role in neurodegenerative disorders and in neural degeneration. Furthermore, elevated expression of this gene product within the frontal cortex of the brain indicates that it may be involved in neuronal survival; synapse formation; conductance; neural differentiation, etc. Such involvement may impact many processes, such as learning and cognition. It may also be useful in the treatment of

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such neurodegenerative disorders as schizophrenia; ALS; or Alzheimer's. Protein, as well as, antibodies directed against the protein may show utility as a tissue-specific marker and/or immunotherapy target for the above listed tissues.

Many polynucleotide sequences, such as EST sequences, are publicly available and accessible through sequence databases. Some of these sequences are related to SEQ ID NO:129 and may have been publicly available prior to conception of the present invention. Preferably, such related polynucleotides are specifically excluded from the scope of the present invention. To list every related sequence is cumbersome. Accordingly, preferably excluded from the present invention are one or more polynucleotides comprising a nucleotide sequence described by the general formula of a-b, where a is any integer between 1 to 1261 of SEQ ID NO:129, b is an integer of 15 to 1275, where both a and b correspond to the positions of nucleotide residues shown in SEQ ID NO:129, and where b is greater than or equal to a + 14.

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FEATURES OF PROTEIN ENCODED BY GENE NO: 120

The translation product of this gene shares homology to a hypothetical protein in Schizosaccharomyces pombe (See Genbank Accession No. 2281980).

In specific embodiments, polypeptides of the invention comprise, or alternatively consists of, an amino acid sequence selected from the group: IYHLHSWIFFHFKRAFCMCFITMKVIHAHCSKLRKCXNAQIS VFCTTLTASYPT (SEQ ID NO:975), IYHLHSWIFFHFKRAFCMCFITM (SEQ ID NO:976), and/or KVIHAHCSKLRKCXNAQISVFCTTLTASYPT (SEQ ID NO:977). Moreover, fragments and variants of these polypeptides (such as, for example, fragments as described herein, polypeptides at least 80%, 85%, 90%, 95%, 96%, 97%, 98%, or 99% identical to these polypeptides and polypeptides encoded by the polynucleotide which hybridizes, under stringent conditions, to the polynucleotide encoding these polypeptides) are encompassed by the invention. Antibodies that bind polypeptides of the invention are also encompassed by the invention. Polynucleotides encoding these polypeptides are also encompassed by the invention.

The gene encoding the disclosed cDNA is thought to reside on chromosome 18. Accordingly, polynucleotides related to this invention are useful as a marker in linkage analysis for chromosome 18.

This gene is expressed primarily in adult hypothalamus and to a lesser extent in infant brain.

Polynucleotides and polypeptides of the invention are useful as reagents for differential identification of the tissue(s) or cell type(s) present in a biological sample and for diagnosis of diseases and conditions which include, but are not limited to, neurodegenerative disorders; endocrine function; and vertigo. Similarly, polypeptides and antibodies directed to these polypeptides are useful in providing immunological probes for differential identification of the tissue(s) or cell type(s). For a number of disorders of the above tissues or cells, particularly of the brain, CNS and peripheral nervous system, expression of this gene at significantly higher or lower levels may be routinely detected in certain tissues or cell types (e.g. brain, cancerous and wounded tissues) or bodily fluids (e.g., lymph, serum, plasma, urine, synovial fluid and spinal fluid) or another tissue or cell sample taken from an individual having such a disorder, relative to the standard gene expression level, i.e., the expression level in healthy tissue or bodily fluid from an individual not having the disorder.

The tissue distribution in adult hypothalamus and infant brain indicates that the protein product of this gene is useful for the treatment and diagnosis of neurodegenerative disorders; diagnosis of tumors of a brain or neuronal origin; treatments involving hormonal control of the entire body and of homeostasis, behavioral disorders, such as Alzheimer's Disease, Parkinson's Disease, Huntington's Disease, schizophrenia, mania, dementia, paranoia, obsessive compulsive disorder and panic disorder. In addition, the gene or gene product may also play a role in the treatment and/or detection of developmental disorders associated with the developing embryo. Protein, as well as, antibodies directed against the protein may show utility as a tissue-specific marker and/or immunotherapy target for the above listed tissues.

Many polynucleotide sequences, such as EST sequences, are publicly available and accessible through sequence databases. Some of these sequences are related to SEQ ID NO:130 and may have been publicly available prior to conception of the present invention. Preferably, such related polynucleotides are specifically

excluded from the scope of the present invention. To list every related sequence is cumbersome. Accordingly, preferably excluded from the present invention are one or more polynucleotides comprising a nucleotide sequence described by the general formula of a-b, where a is any integer between 1 to 458 of SEQ ID NO:130, b is an integer of 15 to 472, where both a and b correspond to the positions of nucleotide residues shown in SEQ ID NO:130, and where b is greater than or equal to a + 14.

FEATURES OF PROTEIN ENCODED BY GENE NO: 121

The translation product of this gene shares sequence homology with the human IRLB protein which is thought to be important in binding to a c-myc promoter element and thus regulating its transcription (See Genbank Accession No. gi|33969). The gene encoding the disclosed cDNA is thought to reside on chromosome 1. Accordingly, polynucleotides related to this invention are useful as a marker in linkage analysis for chromosome 1.

In specific embodiments, polypeptides of the invention comprise, or alternatively consists of, an amino acid sequence selected from the group: WNLLWYFQRLRLPSILPGLVLASCDGPSXSQAPSPWLTPDPASVQVRLLWDV LTPDPN (SEQ ID NO:978), QRGIYREILFLTMAALGKDHVDIVAFDKKYKSAF NKLASSMGKEELRHRRAQMP (SEQ ID NO:979), and/or WNLLWYFQRLRLP SILPGLVLAS (SEQ ID NO:980). Moreover, fragments and variants of these polypeptides (such as, for example, fragments as described herein, polypeptides at least 80%, 85%, 90%, 95%, 96%, 97%, 98%, or 99% identical to these polypeptides and polypeptides encoded by the polynucleotide which hybridizes, under stringent conditions, to the polynucleotide encoding these polypeptides) are encompassed by the invention. Antibodies that bind polypeptides of the invention are also encompassed by the invention. Polynucleotides encoding these polypeptides are also encompassed by the invention.

This gene is expressed primarily in brain and breast, and to a lesser extent in a variety of hematopoietic tissues and cells.

Polynucleotides and polypeptides of the invention are useful as reagents for differential identification of the tissue(s) or cell type(s) present in a biological sample and for diagnosis of diseases and conditions which include, but are not limited to, cancer of the brain and breast; lymphoproliferative disorders; neurodegenerative diseases. Similarly, polypeptides and antibodies directed to these polypeptides are useful in providing immunological probes for differential identification of the tissue(s) or cell type(s). For a number of disorders of the above tissues or cells, particularly of the CNS, breast, and immune system, expression of this gene at significantly higher or lower levels may be routinely detected in certain tissues or cell types (e.g. brain, breast, immune, cancerous and wounded tissues) or bodily fluids (e.g., lymph, serum, plasma, urine, synovial fluid and spinal fluid) or another tissue or cell sample taken from an individual having such a disorder, relative to the standard gene expression level, i.e., the expression level in healthy tissue or bodily fluid from an individual not having the disorder.

The tissue distribution in brain indicates that the protein product of this gene is useful for the treatment and diagnosis of cancer of the brain, breast, and hematopoietic system. In addition, it is useful for the treatment of neurodegenerative disorders, as well as disorders of the hematopoietic system, including defects in immune competency and inflammation. Protein, as well as, antibodies directed against the protein may show utility as a tumor marker and immunotherapy targets for the above listed tumors and tissues.

Many polynucleotide sequences, such as EST sequences, are publicly available and accessible through sequence databases. Some of these sequences are related to SEQ ID NO:131 and may have been publicly available prior to conception of the present invention. Preferably, such related polynucleotides are specifically excluded from the scope of the present invention. To list every related sequence is cumbersome. Accordingly, preferably excluded from the present invention are one or more polynucleotides comprising a nucleotide sequence described by the general formula of a-b, where a is any integer between 1 to 1936 of SEQ ID NO:131, b is an integer of 15 to 1950, where both a and b correspond to the positions of nucleotide residues shown in SEQ ID NO:131, and where b is greater than or equal to a + 14.

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FEATURES OF PROTEIN ENCODED BY GENE NO: 122

The translation product of this gene shares sequence homology with an ATP synthase, a key component of the proton channel that is thought to be important in the translocation of protons across the membrane.

This gene is expressed primarily in T-cell lymphoma.

Polynucleotides and polypeptides of the invention are useful as reagents for differential identification of the tissue(s) or cell type(s) present in a biological sample and for diagnosis of diseases and conditions which include, but are not limited to, T cell lymphoma. Similarly, polypeptides and antibodies directed to these polypeptides are useful in providing immunological probes for differential identification of the tissue(s) or cell type(s). For a number of disorders of the above tissues or cells, particularly of the immune system, expression of this gene at significantly higher or lower levels may be routinely detected in certain tissues or cell types (e.g. immune, cancerous and wounded tissues) or bodily fluids (e.g., lymph, serum, plasma, urine, synovial fluid and spinal fluid) or another tissue or cell sample taken from an individual having such a disorder, relative to the standard gene expression level, i.e., the expression level in healthy tissue or bodily fluid from an individual not having the disorder.

The tissue distribution in T-cell lymphoma, combined with the homology to an ATP synthase indicates that the protein product of this gene is useful for the treatment of defects in proton transport, homeostasis, and metabolism, as well as the diagnosis and treatment of lymphoma. Because the gene is expressed in cells of lymphoid origin, the natural gene product may be involved in immune functions. Therefore it may be also used as an agent for immunological disorders including arthritis, asthma, immune deficiency diseases such as AIDS, and leukemia. Protein, as well as, antibodies directed against the protein may show utility as a tumor marker and/or immunotherapy targets for the above listed tissues.

Many polynucleotide sequences, such as EST sequences, are publicly available and accessible through sequence databases. Some of these sequences are related to SEQ ID NO:132 and may have been publicly available prior to conception

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of the present invention. Preferably, such related polynucleotides are specifically excluded from the scope of the present invention. To list every related sequence is cumbersome. Accordingly, preferably excluded from the present invention are one or more polynucleotides comprising a nucleotide sequence described by the general formula of a-b, where a is any integer between 1 to 976 of SEQ ID NO:132, b is an integer of 15 to 990, where both a and b correspond to the positions of nucleotide residues shown in SEQ ID NO:132, and where b is greater than or equal to a + 14.

FEATURES OF PROTEIN ENCODED BY GENE NO: 123

The gene encoding the disclosed cDNA is thought to reside on chromosome 15. Accordingly, polynucleotides related to this invention are useful as a marker in linkage analysis for chromosome 15.

This gene is expressed primarily in a variety of fetal tissues, including fetal liver, lung, and spleen, and to a lesser extent in a variety of blood cells, including eosinophils and T cells.

Polynucleotides and polypeptides of the invention are useful as reagents for differential identification of the tissue(s) or cell type(s) present in a biological sample and for diagnosis of diseases and conditions which include, but are not limited to, cancer (abnormal cell proliferation); T cell lymphomas; and hematopoietic disorders. Similarly, polypeptides and antibodies directed to these polypeptides are useful in providing immunological probes for differential identification of the tissue(s) or cell type(s). For a number of disorders of the above tissues or cells, particularly of the fetus and immune system, expression of this gene at significantly higher or lower levels may be routinely detected in certain tissues or cell types (e.g. fetal, immune, cancerous and wounded tissues) or bodily fluids (e.g., lymph, serum, plasma, urine, synovial fluid and spinal fluid) or another tissue or cell sample taken from an individual having such a disorder, relative to the standard gene expression level, i.e., the expression level in healthy tissue or bodily fluid from an individual not having the disorder.

The tissue distribution in fetal tissues indicates that the protein product of this gene is useful for the treatment and diagnosis of conditions involving cell proliferation. Similarly, the fetal tissue expression, as well as the expression in a variety of blood cell lineages, indicates that it may play a role in either cellular proliferation, apoptosis, or cell survival. Thus it may be useful in the management and treatment of a variety of cancers and malignancies. In addition, its expression in blood cells indicates that it may play additional roles in hematopoietic disorders and conditions, and could be useful in treating diseases involving autoimmunity, immune modulation, immune surveillance, and inflammation. Protein, as well as, antibodies directed against the protein may show utility as a tumor marker and/or immunotherapy targets for the above listed tissues.

Many polynucleotide sequences, such as EST sequences, are publicly available and accessible through sequence databases. Some of these sequences are related to SEQ ID NO:133 and may have been publicly available prior to conception of the present invention. Preferably, such related polynucleotides are specifically excluded from the scope of the present invention. To list every related sequence is cumbersome. Accordingly, preferably excluded from the present invention are one or more polynucleotides comprising a nucleotide sequence described by the general formula of a-b, where a is any integer between 1 to 1706 of SEQ ID NO:133, b is an integer of 15 to 1720, where both a and b correspond to the positions of nucleotide residues shown in SEQ ID NO:133, and where b is greater than or equal to a + 14.

FEATURES OF PROTEIN ENCODED BY GENE NO: 124

This gene is expressed primarily in placenta, and to a lesser extent in pineal gland and rhabdomyosarcoma.

Polynucleotides and polypeptides of the invention are useful as reagents for differential identification of the tissue(s) or cell type(s) present in a biological sample and for diagnosis of diseases and conditions which include, but are not limited to, developmental, endocrine, and female reproductive disorders. Similarly, polypeptides and antibodies directed to these polypeptides are useful in providing immunological

probes for differential identification of the tissue(s) or cell type(s). For a number of disorders of the above tissues or cells, particularly of the placenta and endocrine system, expression of this gene at significantly higher or lower levels may be routinely detected in certain tissues or cell types (e.g. placental, endocrine, cancerous and wounded tissues) or bodily fluids (e.g., lymph, serum, plasma, urine, synovial fluid and spinal fluid) or another tissue or cell sample taken from an individual having such a disorder, relative to the standard gene expression level, i.e., the expression level in healthy tissue or bodily fluid from an individual not having the disorder.

Predicted epitopes include those comprising a sequence shown in SEQ ID NO: 372 as residues: Leu-69 to Val-76.

The tissue distribution in placenta indicates that the protein product of this gene is useful for the diagnosis and treatment of developmental disorders. Furthermore, the tissue distribution indicates that the protein product of this gene is useful for the diagnosis and/or treatment of disorders of the placenta. Specific expression within the placenta indicates that this gene product may play a role in the proper establishment and maintenance of placental function. Alternately, this gene product may be produced by the placenta and then transported to the embryo, where it may play a crucial role in the development and/or survival of the developing embryo or fetus. Expression of this gene product in a vascular-rich tissue such as the placenta also indicates that this gene product may be produced more generally in endothelial cells or within the circulation. In such instances, it may play more generalized roles in vascular function, such as in angiogenesis. It may also be produced in the vasculature and have effects on other cells within the circulation, such as hematopoietic cells. It may serve to promote the proliferation, survival, activation, and/or differentiation of hematopoietic cells, as well as other cells throughout the body. Protein, as well as, antibodies directed against the protein may show utility as a tissue-specific marker and/or immunotherapy target for the above listed tissues.

Many polynucleotide sequences, such as EST sequences, are publicly available and accessible through sequence databases. Some of these sequences are related to SEQ ID NO:134 and may have been publicly available prior to conception of the present invention. Preferably, such related polynucleotides are specifically excluded from the scope of the present invention. To list every related sequence is

cumbersome. Accordingly, preferably excluded from the present invention are one or more polynucleotides comprising a nucleotide sequence described by the general formula of a-b, where a is any integer between 1 to 691 of SEQ ID NO:134, b is an integer of 15 to 705, where both a and b correspond to the positions of nucleotide residues shown in SEQ ID NO:134, and where b is greater than or equal to a + 14.

FEATURES OF PROTEIN ENCODED BY GENE NO: 125

Contact of cells with supernatant expressing the product of this gene increases the permeability of THP-1 Monocyte cells to calcium. Thus, it is likely that the product of this gene is involved in a signal transduction pathway that is initiated when the product of this gene binds a receptor on the surface of the Monocyte cell. Thus, polynucleotides and polypeptides have uses which include, but are not limited to, activating monocyte cells.

This gene is expressed primarily in benign prostatic hyperplasia.

Polynucleotides and polypeptides of the invention are useful as reagents for differential identification of the tissue(s) or cell type(s) present in a biological sample and for diagnosis of benign prostatic hyperplasia. Similarly, polypeptides and antibodies directed to these polypeptides are useful in providing immunological probes for differential identification of the tissue(s) or cell type(s). For a number of disorders of the above tissues or cells, particularly of the reproductive system, expression of this gene at significantly higher or lower levels may be routinely detected in certain tissues or cell types (e.g. reproductive, cancerous and wounded tissues) or bodily fluids (e.g., lymph, serum, plasma, urine, synovial fluid and spinal fluid) or another tissue or cell sample taken from an individual having such a disorder, relative to the standard gene expression level, i.e., the expression level in healthy tissue or bodily fluid from an individual not having the disorder.

The tissue distribution in benign prostatic hyperplasia tissue indicates that the protein product of this gene is useful for the treatment and diagnosis of proliferative disorders of the prostate. Furthermore, the biological activity data indicates that the translation product of this gene is useful for the stimulation of certain immune system

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cells, such as monocytes, which may be useful for helping the body to defend against infection. Protein, as well as, antibodies directed against the protein may show utility as a tumor marker and immunotherapy targets for the above listed tumors and tissues.

Many polynucleotide sequences, such as EST sequences, are publicly available and accessible through sequence databases. Some of these sequences are related to SEQ ID NO:135 and may have been publicly available prior to conception of the present invention. Preferably, such related polynucleotides are specifically excluded from the scope of the present invention. To list every related sequence is cumbersome. Accordingly, preferably excluded from the present invention are one or more polynucleotides comprising a nucleotide sequence described by the general formula of a-b, where a is any integer between 1 to 309 of SEQ ID NO:135, b is an integer of 15 to 323, where both a and b correspond to the positions of nucleotide residues shown in SEQ ID NO:135, and where b is greater than or equal to a + 14.

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FEATURES OF PROTEIN ENCODED BY GENE NO: 126

This gene is expressed primarily in Raji cells.

Polynucleotides and polypeptides of the invention are useful as reagents for differential identification of the tissue(s) or cell type(s) present in a biological sample and for diagnosis of diseases and conditions which include, but are not limited to, inflammation and T cell autoimmune disorders. Similarly, polypeptides and antibodies directed to these polypeptides are useful in providing immunological probes for differential identification of the tissue(s) or cell type(s). For a number of disorders of the above tissues or cells, particularly of the immune system, expression of this gene at significantly higher or lower levels may be routinely detected in certain tissues or cell types (e.g., cancerous and wounded tissues) or bodily fluids (e.g., lymph, serum, plasma, urine, synovial fluid and spinal fluid) or another tissue or cell sample taken from an individual having such a disorder, relative to the standard gene expression level, i.e., the expression level in healthy tissue or bodily fluid from an individual not having the disorder.

The tissue distribution in Raji cells indicates that the protein product of this gene is useful for treatment and diagnosis of inflammation and T cell autoimmune disorders. Because the gene is expressed in cells of lymphoid origin, the natural gene product may be involved in immune functions. Therefore it may be also used as an agent for immunological disorders including arthritis, asthma, immune deficiency diseases (such as AIDS), and leukemia. Protein, as well as, antibodies directed against the protein may show utility as a tumor marker and/or immunotherapy targets for the above listed tissues.

Many polynucleotide sequences, such as EST sequences, are publicly available and accessible through sequence databases. Some of these sequences are related to SEQ ID NO:136 and may have been publicly available prior to conception of the present invention. Preferably, such related polynucleotides are specifically excluded from the scope of the present invention. To list every related sequence is cumbersome. Accordingly, preferably excluded from the present invention are one or more polynucleotides comprising a nucleotide sequence described by the general formula of a-b, where a is any integer between 1 to 568 of SEQ ID NO:136, b is an integer of 15 to 582, where both a and b correspond to the positions of nucleotide residues shown in SEQ ID NO:136, and where b is greater than or equal to a + 14.

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FEATURES OF PROTEIN ENCODED BY GENE NO: 127

This gene is expressed primarily in apoptotic T-cells, and to a lesser extent in suppressor T cells and ulcerative colitis.

Polynucleotides and polypeptides of the invention are useful as reagents for differential identification of the tissue(s) or cell type(s) present in a biological sample and for diagnosis of diseases and conditions which include, but are not limited to, diseases involving premature apoptosis, and immunological and gastrointestinal disorders. Similarly, polypeptides and antibodies directed to these polypeptides are useful in providing immunological probes for differential identification of the tissue(s) or cell type(s). For a number of disorders of the above tissues or cells, particularly of the immune system, expression of this gene at significantly higher or

lower levels may be routinely detected in certain tissues or cell types (e.g. immune, gastrointestinal, cancerous and wounded tissues) or bodily fluids (e.g., lymph, serum, plasma, urine, synovial fluid and spinal fluid) or another tissue or cell sample taken from an individual having such a disorder, relative to the standard gene expression level, i.e., the expression level in healthy tissue or bodily fluid from an individual not having the disorder.

Predicted epitopes include those comprising a sequence shown in SEQ ID NO: 375 as residues: Asp-23 to Gly-29.

The tissue distribution in apoptotic T-cells indicates that the protein product of this gene is useful for the treatment and diagnosis of disorders involving inappropriate levels of apoptosis, especially in immune cell lineages. Because the gene is expressed in cells of lymphoid origin, the natural gene product may be involved in immune functions. Therefore it may be also used as an agent for immunological disorders including arthritis, asthma, immune deficiency diseases (such as AIDS), and leukemia. Furthermore, expression of this gene product in T cells also strongly indicates a role for this protein in immune function and immune surveillance. Protein, as well as, antibodies directed against the protein may show utility as a tumor marker and/or immunotherapy targets for the above listed tissues.

Many polynucleotide sequences, such as EST sequences, are publicly available and accessible through sequence databases. Some of these sequences are related to SEQ ID NO:137 and may have been publicly available prior to conception of the present invention. Preferably, such related polynucleotides are specifically excluded from the scope of the present invention. To list every related sequence is cumbersome. Accordingly, preferably excluded from the present invention are one or more polynucleotides comprising a nucleotide sequence described by the general formula of a-b, where a is any integer between 1 to 1007 of SEQ ID NO:137, b is an integer of 15 to 1021, where both a and b correspond to the positions of nucleotide residues shown in SEQ ID NO:137, and where b is greater than or equal to a + 14.

FEATURES OF PROTEIN ENCODED BY GENE NO: 128

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The translation product of this gene shares sequence homology with an C. elegans coding region C47D12.2 of unknown function (See Genbank Accession No. gnl|PID|e348986).

In specific embodiments, polypeptides of the invention comprise, or alternatively consists of, an amino acid sequence selected from the group: EDDGFNRSIHEVILKNITWYSERVLTEISLGSLLILVVIRTIQYNMTRTRDKYLH TNCLAALANMSAQFRSLHQYAAQRIISLFSLLSKKHNKVLEQATQSLRGSLSS NDVPLPDYAQDLNVIEEVIRMMLEIINSCLTNSLHHNPNLVYALLYKRDLFEQ FRTHPSFQDIMQNIDLVISFFSSRLLQAGS (SEQ ID NO:981), EDDGFNRSIHEVILKNITWYSERVLTEISLGSLLILVV (SEQ ID NO:982), RTIQYNMTRTRDKYLHTNCLAALANMSAQFRSLHQYAAQRIISLFSLLSKKH N (SEQ ID NO:983), SCLTNSLHHNPNLVYALLYKRDLFEQFRTHPSFQDIMQNIDLVISFFSSRLLQA GS (SEQ ID NO:984), KKHNKVLEQATQSLRGSLSSNDVPLPDYAQD (SEQ ID NO:985), TISNSSFISGYNAKY (SEQ ID NO:986), and/or LKVAASWELSCQWNGSWKSLSKASLRC PKTD (SEQ ID NO:987). Moreover, fragments and variants of these polypeptides (such as, for example, fragments as described herein, polypeptides at least 80%, 85%, 90%, 95%, 96%, 97%, 98%, or 99% identical to these polypeptides and polypeptides encoded by the polynucleotide which hybridizes, under stringent conditions, to the polynucleotide encoding these polypeptides) are encompassed by the invention. Antibodies that bind polypeptides of the invention are also encompassed by the invention. Polynucleotides encoding these polypeptides are also encompassed by the invention.

The gene encoding the disclosed cDNA is thought to reside on chromosome 18. Accordingly, polynucleotides related to this invention are useful as a marker in linkage analysis for chromosome 18.

This gene is expressed primarily in smooth muscle, and to a lesser extent in fetal liver/spleen.

Polynucleotides and polypeptides of the invention are useful as reagents for differential identification of the tissue(s) or cell type(s) present in a biological sample and for diagnosis of diseases and conditions which include, but are not limited to, atherosclerosis and other cardiovascular and hepatic disorders. Similarly,

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polypeptides and antibodies directed to these polypeptides are useful in providing immunological probes for differential identification of the tissue(s) or cell type(s). For a number of disorders of the above tissues or cells, particularly of the circulatory system, expression of this gene at significantly higher or lower levels may be routinely detected in certain tissues or cell types (e.g. muscle, fetal liver/spleen, cancerous and wounded tissues) or bodily fluids (e.g., lymph, serum, plasma, urine, synovial fluid and spinal fluid) or another tissue or cell sample taken from an individual having such a disorder, relative to the standard gene expression level, i.e., the expression level in healthy tissue or bodily fluid from an individual not having the disorder.

The tissue distribution in smooth muscle indicates that the protein product of this gene is useful for the diagnosis and treatment of circulatory system disorders such as atherosclerosis, hypertension, stroke, aneurysms, embolisms, and thrombosis. In addition, the tissue distribution indicates that the protein product of this gene is useful for the detection and treatment of liver disorders and cancers (e.g. hepatoblastoma, jaundice, hepatitis, liver metabolic diseases and conditions that are attributable to the differentiation of hepatocyte progenitor cells). In addition the expression in fetus indicates a useful role for the protein product in developmental abnormalities, fetal deficiencies, pre-natal disorders and various would-healing models and/or tissue trauma. Protein, as well as, antibodies directed against the protein may show utility as a tumor marker and/or immunotherapy targets for the above listed tissues.

Many polynucleotide sequences, such as EST sequences, are publicly available and accessible through sequence databases. Some of these sequences are related to SEQ ID NO:138 and may have been publicly available prior to conception of the present invention. Preferably, such related polynucleotides are specifically excluded from the scope of the present invention. To list every related sequence is cumbersome. Accordingly, preferably excluded from the present invention are one or more polynucleotides comprising a nucleotide sequence described by the general formula of a-b, where a is any integer between 1 to 1763 of SEQ ID NO:138, b is an integer of 15 to 1777, where both a and b correspond to the positions of nucleotide residues shown in SEQ ID NO:138, and where b is greater than or equal to a + 14.

FEATURES OF PROTEIN ENCODED BY GENE NO: 129

The translation product of this gene shares sequence homology with a ribosomal protein which is thought to be important in cellular metabolism, in addition to the C.elegans protein F40F11.1 which does not have a known function at the current time (See Genbank Accession No. gnl|PID|e244552).

In specific embodiments, polypeptides of the invention comprise, or alternatively consists of, an amino acid sequence selected from the group: MADIQTERAYQKQPTIFQNKKRVLLGETGKEKLPRVTNKNIGLGFKDTPRRL LRGTYIDKKCPFTGNVSIRGRILSGVVTQDEDAEDHCHPPRLSALHPQVQPLR EAPQEHVCTPVPLLQGRPDR (SEQ ID NO:988), MKMQRTIVIRRDYLHYIRKYNRFEKRHKNMSVHLSPCFRDVQIGDIVTVGEC RPLSKTVRFNVLKVTKAAGTKKQFQKF (SEQ ID NO:989), MADIQTERAYQKQPTIFQNKKRVLLGETGK (SEQ ID NO:990), KLPRVTNKNIGLGFKDTPRRLLRGTYIDKKCPFTGNVSIRGRILSGVVTQDED AEDHC (SEQ ID NO:991), HCHPPRLSALHPQVQPLREAPQEHVCTPVPLLQGRPDR (SEQ ID NO:992), MKMQRTIVIRRDYLHYIRKYNRFEKRHKNMSVHLSP (SEQ ID NO:993), CFRDVQIGDIVTVGECRPLSKTVRFNVLKVTKAAGTKKQFQKF (SEQ ID NO:994), PRRLLRGTYIDKKCPFTGNVSIRGRILSGVVTQ (SEQ ID NO:995), SRGTGVQTCSCGASRSGCTCGCSADSLGG (SEQ ID NO:996), and/or QWSSASSSWVTTPERIRPRMDTLPVKGHFLSM (SEQ ID NO:997). Moreover, fragments and variants of these polypeptides (such as, for example, fragments as described herein, polypeptides at least 80%, 85%, 90%, 95%, 96%, 97%, 98%, or 99% identical to these polypeptides and polypeptides encoded by the polynucleotide which hybridizes, under stringent conditions, to the polynucleotide encoding these polypeptides) are encompassed by the invention. Antibodies that bind polypeptides of the invention are also encompassed by the invention. Polynucleotides encoding these polypeptides are also encompassed by the invention.

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The gene encoding the disclosed cDNA is thought to reside on chromosome 19. Accordingly, polynucleotides related to this invention are useful as a marker in linkage analysis for chromosome 19.

This gene is expressed primarily in Wilm's tumor, and to a lesser extent in thymus and stromal cells.

Polynucleotides and polypeptides of the invention are useful as reagents for differential identification of the tissue(s) or cell type(s) present in a biological sample and for diagnosis of diseases and conditions which include, but are not limited to, Kidney disorders and cancer, diseases affecting RNA translation. Similarly, polypeptides and antibodies directed to these polypeptides are useful in providing immunological probes for differential identification of the tissue(s) or cell type(s). For a number of disorders of the above tissues or cells, particularly of the Wilm's tumors, expression of this gene at significantly higher or lower levels may be routinely detected in certain tissues or cell types (e.g. kidney, thymus, cancerous and wounded tissues) or bodily fluids (e.g., lymph, serum, plasma, urine, synovial fluid and spinal fluid) or another tissue or cell sample taken from an individual having such a disorder, relative to the standard gene expression level, i.e., the expression level in healthy tissue or bodily fluid from an individual not having the disorder.

Predicted epitopes include those comprising a sequence shown in SEQ ID NO: 377 as residues: Arg-15 to Gly-22.

The tissue distribution in Wilm's tumor, combined with the homology to a ribosomal protein indicates that the protein product of this gene is useful for diseases affecting RNA translation, in addition to proliferative disorders. Furthermore, given the tissue distribution, the translation product of this gene may be useful in treating and/or detecting Wilm's tumor or tumors of other tissues mentioned previously. Protein, as well as, antibodies directed against the protein may show utility as a tumor marker and/or immunotherapy targets for the above listed tissues.

Many polynucleotide sequences, such as EST sequences, are publicly available and accessible through sequence databases. Some of these sequences are related to SEQ ID NO:139 and may have been publicly available prior to conception of the present invention. Preferably, such related polynucleotides are specifically excluded from the scope of the present invention. To list every related sequence is

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cumbersome. Accordingly, preferably excluded from the present invention are one or more polynucleotides comprising a nucleotide sequence described by the general formula of a-b, where a is any integer between 1 to 629 of SEQ ID NO:139, b is an integer of 15 to 643, where both a and b correspond to the positions of nucleotide residues shown in SEQ ID NO:139, and where b is greater than or equal to a + 14.

FEATURES OF PROTEIN ENCODED BY GENE NO: 130

The translation product of this gene shares sequence homology with a yeast DNA helicase, which is thought to be important in global transcriptional regulation (See Genbank Accession No. gnl|PID|e243594).

In specific embodiments, polypeptides of the invention comprise, or alternatively consists of, an amino acid sequence selected from the group: IFYDSDWNPTVDQQAMDRAHRLGQTKQVTVYRLICKGTIEERILQRAKEKSEI QRMVISG (SEQ ID NO:998), TRMIDLLEEYMVYRKHTYXRLDGSSKISERRDMVADFQNRNDIFVFLLSTRA GGLGINLTAXDTVHF (SEQ ID NO:999), IFYDSDWNPTVDQQAMDRAHRLGQTKQVTVYR (SEQ ID NO:1000), VYRLICKGTIEERILQRAKEKSEIQRMVISG (SEQ ID NO:1001), TRMIDLLEEYMVYRKHTYXRLDGSSKISERRDM (SEQ ID NO:1002), RRDMVADFQNRNDIFVFLLSTRAGGLGINLTAXDTVHF (SEQ ID NO:1003), IFYDSDWNPTVDQQAMDRAHRLGQTKQVTVYRLICKG (SEQ ID NO:1004), IFYDSDWNPTVDQQAMDRAHRLGQTKQVTVYRLICKG (SEQ ID NO:1005), RLICKGTIEERILQRAKEKSEIQRMVISG (SEQ ID NO:1006), and/or GTRMIDLLEEYMVYRKHTYXRLDGSSKISERRDMVADFQNRNDIFVFLLSTR AGGLGINLTAXDTVHFL (SEQ ID NO:1007). Moreover, fragments and variants of these polypeptides (such as, for example, fragments as described herein, polypeptides at least 80%, 85%, 90%, 95%, 96%, 97%, 98%, or 99% identical to these polypeptides and polypeptides encoded by the polynucleotide which hybridizes, under stringent conditions, to the polynucleotide encoding these polypeptides) are encompassed by the invention. Antibodies that bind polypeptides of the invention are

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also encompassed by the invention. Polynucleotides encoding these polypeptides are also encompassed by the invention.

This gene is expressed primarily in amygdala.

Polynucleotides and polypeptides of the invention are useful as reagents for differential identification of the tissue(s) or cell type(s) present in a biological sample and for diagnosis of diseases and conditions which include, but are not limited to, diseases and disorders of the brain and the endocrine system. Similarly, polypeptides and antibodies directed to these polypeptides are useful in providing immunological probes for differential identification of the tissue(s) or cell type(s). For a number of disorders of the above tissues or cells, particularly of the central nervous system, endocrine system, expression of this gene at significantly higher or lower levels may be routinely detected in certain tissues or cell types (e.g. brain, endocrine, cancerous and wounded tissues) or bodily fluids (e.g., lymph, serum, plasma, urine, synovial fluid and spinal fluid) or another tissue or cell sample taken from an individual having such a disorder, relative to the standard gene expression level, i.e., the expression level in healthy tissue or bodily fluid from an individual not having the disorder.

Predicted epitopes include those comprising a sequence shown in SEQ ID NO: 378 as residues: Lys-24 to Tyr-34.

The tissue distribution in amygdala, combined with the homology to a DNA helicase indicates that the protein product of this gene is useful for diseases affecting RNA transcription, particularly developmental disorders and healing wounds, since the later are thought to approximate developmental transcriptional regulation. The amygdala processes sensory information and relays this to other areas of the brain including the endocrine and autonomic domains of the hypothalamus and the brain stem. Therefore, the translation product of this gene is also useful for the detection and/or treatment of disorders of the endocrine and/or neural systems. Protein, as well as, antibodies directed against the protein may show utility as a tissue-specific marker and/or immunotherapy target for the above listed tissues.

Many polynucleotide sequences, such as EST sequences, are publicly available and accessible through sequence databases. Some of these sequences are related to SEQ ID NO:140 and may have been publicly available prior to conception of the present invention. Preferably, such related polynucleotides are specifically

excluded from the scope of the present invention. To list every related sequence is cumbersome. Accordingly, preferably excluded from the present invention are one or more polynucleotides comprising a nucleotide sequence described by the general formula of a-b, where a is any integer between 1 to 1206 of SEQ ID NO:140, b is an integer of 15 to 1220, where both a and b correspond to the positions of nucleotide residues shown in SEQ ID NO:140, and where b is greater than or equal to a + 14.

FEATURES OF PROTEIN ENCODED BY GENE NO: 131

This gene is expressed primarily in prostate, and to a lesser extent in amygdala and pancreatic tumors.

Polynucleotides and polypeptides of the invention are useful as reagents for differential identification of the tissue(s) or cell type(s) present in a biological sample and for diagnosis of diseases and conditions which include, but are not limited to, prostate enlargement and gastrointestinal disorders, particularly of the pancreas and gall bladder. Similarly, polypeptides and antibodies directed to these polypeptides are useful in providing immunological probes for differential identification of the tissue(s) or cell type(s). For a number of disorders of the above tissues or cells, particularly of the reproductive system, expression of this gene at significantly higher or lower levels may be routinely detected in certain tissues or cell types (e.g. reproductive, cancerous and wounded tissues) or bodily fluids (e.g., lymph, serum, plasma, urine, synovial fluid and spinal fluid) or another tissue or cell sample taken from an individual having such a disorder, relative to the standard gene expression level, i.e., the expression level in healthy tissue or bodily fluid from an individual not having the disorder.

The tissue distribution in prostate indicates that the protein product of this gene is useful for the treatment and diagnosis of prostate or reproductive diseases, including benign prostatic hyperplasia and prostate cancer. In addition, the tissue distribution in tumors of the pancreas indicates that the protein product of this gene is useful for the diagnosis and intervention of these tumors, in addition to other tissues where expression has been indicated. Protein, as well as, antibodies directed against

the protein may show utility as a tumor marker and/or immunotherapy targets for the above listed tumors and tissues.

Many polynucleotide sequences, such as EST sequences, are publicly available and accessible through sequence databases. Some of these sequences are related to SEQ ID NO:141 and may have been publicly available prior to conception of the present invention. Preferably, such related polynucleotides are specifically excluded from the scope of the present invention. To list every related sequence is cumbersome. Accordingly, preferably excluded from the present invention are one or more polynucleotides comprising a nucleotide sequence described by the general formula of a-b, where a is any integer between 1 to 707 of SEQ ID NO:141, b is an integer of 15 to 721, where both a and b correspond to the positions of nucleotide residues shown in SEQ ID NO:141, and where b is greater than or equal to a + 14.

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FEATURES OF PROTEIN ENCODED BY GENE NO: 132

The gene encoding the disclosed cDNA is thought to reside on chromosome 3. Accordingly, polynucleotides related to this invention are useful as a marker in linkage analysis for chromosome 3.

This gene is expressed primarily in adult lung, and to a lesser extent in the hypothalamus.

Polynucleotides and polypeptides of the invention are useful as reagents for differential identification of the tissue(s) or cell type(s) present in a biological sample and for diagnosis of diseases and conditions which include, but are not limited to, pulmonary diseases and neurological disorders. Similarly, polypeptides and antibodies directed to these polypeptides are useful in providing immunological probes for differential identification of the tissue(s) or cell type(s). For a number of disorders of the above tissues or cells, particularly of the pulmonary and respiratory systems, expression of this gene at significantly higher or lower levels may be routinely detected in certain tissues or cell types (e.g. lung, brain, cancerous and wounded tissues) or bodily fluids (e.g., lymph, serum, plasma, urine, synovial fluid and spinal fluid) or another tissue or cell sample taken from an individual having such

a disorder, relative to the standard gene expression level, i.e., the expression level in healthy tissue or bodily fluid from an individual not having the disorder.

The tissue distribution in adult lung indicates that the protein product of this gene is useful for the diagnosis and treatment of pulmonary and respiratory disorders such as emphysema, pneumonia, and pulmonary edema and emboli. In addition, the tissue distribution indicates that the protein product of this gene is useful for the detection/treatment of neurodegenerative disease states and behavioral disorders such as Alzheimer's Disease, Parkinson's Disease, Huntington's Disease, schizophrenia, mania, dementia, paranoia, obsessive compulsive disorder and panic disorder. In addition, the gene or gene product may also play a role in the treatment and/or detection of developmental disorders associated with the developing embryo, sexually-linked disorders, or disorders of the cardiovascular system. Protein, as well as, antibodies directed against the protein may show utility as a tissue-specific marker and/or immunotherapy target for the above listed tissues.

Many polynucleotide sequences, such as EST sequences, are publicly available and accessible through sequence databases. Some of these sequences are related to SEQ ID NO:142 and may have been publicly available prior to conception of the present invention. Preferably, such related polynucleotides are specifically excluded from the scope of the present invention. To list every related sequence is cumbersome. Accordingly, preferably excluded from the present invention are one or more polynucleotides comprising a nucleotide sequence described by the general formula of a-b, where a is any integer between 1 to 1454 of SEQ ID NO:142, b is an integer of 15 to 1468, where both a and b correspond to the positions of nucleotide residues shown in SEQ ID NO:142, and where b is greater than or equal to a + 14.

FEATURES OF PROTEIN ENCODED BY GENE NO: 133

This gene is expressed primarily in human liver.

Polynucleotides and polypeptides of the invention are useful as reagents for differential identification of the tissue(s) or cell type(s) present in a biological sample and for diagnosis of diseases and conditions which include, but are not limited to,

cirrhosis of the liver and other hepatic disorders. Similarly, polypeptides and antibodies directed to these polypeptides are useful in providing immunological probes for differential identification of the tissue(s) or cell type(s). For a number of disorders of the above tissues or cells, particularly of the digestive system, expression of this gene at significantly higher or lower levels may be routinely detected in certain tissues or cell types (e.g. liver, cancerous and wounded tissues) or bodily fluids (e.g., lymph, serum, plasma, urine, synovial fluid and spinal fluid) or another tissue or cell sample taken from an individual having such a disorder, relative to the standard gene expression level, i.e., the expression level in healthy tissue or bodily fluid from an individual not having the disorder.

The tissue distribution in human liver indicates that the protein product of this gene is useful for the detection and treatment of liver disorders and cancers (e.g. hepatoblastoma, jaundice, hepatitis, liver metabolic diseases and conditions that are attributable to the differentiation of hepatocyte progenitor cells). Protein, as well as, antibodies directed against the protein may show utility as a tumor marker and/or immunotherapy targets for the above listed tissues.

Many polynucleotide sequences, such as EST sequences, are publicly available and accessible through sequence databases. Some of these sequences are related to SEQ ID NO:143 and may have been publicly available prior to conception of the present invention. Preferably, such related polynucleotides are specifically excluded from the scope of the present invention. To list every related sequence is cumbersome. Accordingly, preferably excluded from the present invention are one or more polynucleotides comprising a nucleotide sequence described by the general formula of a-b, where a is any integer between 1 to 286 of SEQ ID NO:143, b is an integer of 15 to 300, where both a and b correspond to the positions of nucleotide residues shown in SEQ ID NO:143, and where b is greater than or equal to a + 14.

FEATURES OF PROTEIN ENCODED BY GENE NO: 134

The gene encoding the disclosed cDNA is thought to reside on chromosome 5. Accordingly, polynucleotides related to this invention are useful as a marker in linkage analysis for chromosome 5.

This gene is expressed primarily in fetal kidney, and to a lesser extent in fetal liver and spleen.

Polynucleotides and polypeptides of the invention are useful as reagents for differential identification of the tissue(s) or cell type(s) present in a biological sample and for diagnosis of diseases and conditions which include, but are not limited to, development and regeneration of liver and kidney and immunological disorders. Similarly, polypeptides and antibodies directed to these polypeptides are useful in providing immunological probes for differential identification of the tissue(s) or cell type(s). For a number of disorders of the above tissues or cells, particularly of the digestive and excretory systems, expression of this gene at significantly higher or lower levels may be routinely detected in certain tissues or cell types (e.g. kidney, liver, spleen, cancerous and wounded tissues) or bodily fluids (e.g., lymph, serum, plasma, urine, synovial fluid and spinal fluid) or another tissue or cell sample taken from an individual having such a disorder, relative to the standard gene expression level, i.e., the expression level in healthy tissue or bodily fluid from an individual not having the disorder.

Predicted epitopes include those comprising a sequence shown in SEQ ID NO: 382 as residues: Pro-70 to Arg-77, Tyr-102 to Thr-107.

The tissue distribution in fetal kidney indicates that the protein product of this gene is useful for the diagnosis and treatment of diseases of the kidney and liver, such as cirrhosis, kidney failure, kidney stones, and liver failure, hepatoblastoma, jaundice, hepatitis, liver metabolic diseases and conditions that are attributable to the differentiation of hepatocyte progenitor cells. In addition the expression in fetus would suggest a useful role for the protein product in developmental abnormalities, fetal deficiencies, pre-natal disorders and various would-healing models and/or tissue trauma. Protein, as well as, antibodies directed against the protein may show utility as a tumor marker and/or immunotherapy targets for the above listed tissues.

Many polynucleotide sequences, such as EST sequences, are publicly available and accessible through sequence databases. Some of these sequences are

related to SEQ ID NO:144 and may have been publicly available prior to conception of the present invention. Preferably, such related polynucleotides are specifically excluded from the scope of the present invention. To list every related sequence is cumbersome. Accordingly, preferably excluded from the present invention are one or more polynucleotides comprising a nucleotide sequence described by the general formula of a-b, where a is any integer between 1 to 2229 of SEQ ID NO:144, b is an integer of 15 to 2243, where both a and b correspond to the positions of nucleotide residues shown in SEQ ID NO:144, and where b is greater than or equal to a + 14.

FEATURES OF PROTEIN ENCODED BY GENE NO: 135

This gene is expressed primarily in brain, bone marrow, and to a lesser extent in placenta, T cell, testis and neutrophils.

Polynucleotides and polypeptides of the invention are useful as reagents for differential identification of the tissue(s) or cell type(s) present in a biological sample and for diagnosis of diseases and conditions which include, but are not limited to, neurodegenerative and immunological diseases and cancer. Similarly, polypeptides and antibodies directed to these polypeptides are useful in providing immunological probes for differential identification of the tissue(s) or cell type(s). For a number of disorders of the above tissues or cells, particularly of the nervous and immune systems, expression of this gene at significantly higher or lower levels may be routinely detected in certain tissues or cell types (e.g., CNS, immune, cancerous and wounded tissues) or bodily fluids (e.g., lymph, serum, seminal fluid, plasma, urine, synovial fluid and spinal fluid) or another tissue or cell sample taken from an individual having such a disorder, relative to the standard gene expression level, i.e., the expression level in healthy tissue or bodily fluid from an individual not having the disorder.

Predicted epitopes include those comprising a sequence shown in SEQ ID NO: 383 as residues: Met-1 to His-6.

The tissue distribution in brain indicates that the protein product of this gene is useful for the detection/treatment of neurodegenerative disease states and behavioral

disorders such as Alzheimer's Disease, Parkinson's Disease, Huntington's Disease, schizophrenia, mania, dementia, paranoia, obsessive compulsive disorder and panic disorder. In addition, the gene or gene product may also play a role in the treatment and/or detection of developmental disorders associated with the developing embryo, or sexually-linked disorders. Furthermore, the tissue distribution indicates that the protein product of this gene is useful for the diagnosis and/or treatment of hematopoietic disorders. This gene product is expressed in hematopoietic cells and tissues, suggesting that it plays a role in the survival, proliferation, and/or differentiation of hematopoietic lineages. Expression of this gene product in T cells and neutrophils also strongly indicates a role for this protein in immune function and immune surveillance.

Many polynucleotide sequences, such as EST sequences, are publicly available and accessible through sequence databases. Some of these sequences are related to SEQ ID NO:145 and may have been publicly available prior to conception of the present invention. Preferably, such related polynucleotides are specifically excluded from the scope of the present invention. To list every related sequence is cumbersome. Accordingly, preferably excluded from the present invention are one or more polynucleotides comprising a nucleotide sequence described by the general formula of a-b, where a is any integer between 1 to 1068 of SEQ ID NO:145, b is an integer of 15 to 1082, where both a and b correspond to the positions of nucleotide residues shown in SEQ ID NO:145, and where b is greater than or equal to a + 14.

FEATURES OF PROTEIN ENCODED BY GENE NO: 136

The translation product of this gene is homologous to the human WD repeat protein HAN11, which is thought to function in signal transduction pathways.

In specific embodiments, polypeptides of the invention comprise, or alternatively consists of, an amino acid sequence selected from the group:

MSLHGKRKEIYKYEAPWTVYAMNWSVRPDKRFRLALGSFVEEYNNKVQLV
GLDEESSEFICRNTFDHPYPTTKLMWIPDTKGVYPDLLATSGDYLRVWRVGE
TETRLECLLNNNKNSDFCAPLTSFDWNEVDPYLLGTSSIDTTCTIWGLETGQV

LGRVNLVSGHVKTQLIAHDKEVYDIAFSRAGGGRDMFASVGADGSVRMFDL
RHLEHSTIIYEDPQHHPLLRLCWNKQDPNYLATMAMDGMEVVILDVRVPAH
LXPGTTIEHVSMALLGPHIHPATSALQRMTTRLSSGTSSKCPEPLRTLSWPTQL
XGEINNVQWASTQPELSPSATTTAWRYSECSVGGAVPTRQGLLYFLPLPHPQS
(SEQ ID NO:1008),
MSLHGKRKEIYKYEAPWTVYAMNWSVRPDKRFRLALGSFVEEYNNKVQLV
GLDEESSEFICRNTFDHPYPTTKLMWIPDTKGVYPDLLATSGDYLRVWRVGE
TETRLECLLNNNKNSDFCAPLTSFDWNEVDPYLL (SEQ ID NO:1009),
SFDWNEVDPYLLGTSSIDTTCTIWGLETGQVLGRVNLVSGHVKTQLIAHDKE
VYDIAFSRAGGGRDMFASVGADGSVRMFDLRHLEHSTIIYEDPQHHPLLRLC
WNKQDPNYLATMAMDGMEVVILDVRVPAHLXPGTTI (SEQ ID NO:1010),
and/or VGADGSVRMFDLRHLEHSTIIYEDPQHHPLLRLCWNKQD
PNYLATMAMDGMEVVILDVRVPAHLXPGTTIEHVSMALLGPHIHPATSALQR
MTTRLSSGTSSKCPEPLRTLSWPTQLXGEINNVQWASTQPELSPSATTTAWRY
SECSVGGAVPTRQGLLYFLPLPHPQS (SEQ ID NO:1011). Moreover, fragments and variants of these polypeptides (such as, for example, fragments as described herein, polypeptides at least 80%, 85%, 90%, 95%, 96%, 97%, 98%, or 99% identical to these polypeptides and polypeptides encoded by the polynucleotide which hybridizes, under stringent conditions, to the polynucleotide encoding these polypeptides) are encompassed by the invention. Antibodies that bind polypeptides of the invention are also encompassed by the invention. Polynucleotides encoding these polypeptides are also encompassed by the invention.

The gene encoding the disclosed cDNA is thought to reside on chromosome 17. Accordingly, polynucleotides related to this invention are useful as a marker in linkage analysis for chromosome 17.

This gene is expressed primarily in placenta, embryo, T cell and fetal lung, and to a lesser extent in endothelial, tonsil and bone marrow.

Polynucleotides and polypeptides of the invention are useful as reagents for differential identification of the tissue(s) or cell type(s) present in a biological sample and for diagnosis of diseases and conditions which include, but are not limited to, immunological and developmental diseases in addition to cancers. Similarly, polypeptides and antibodies directed to these polypeptides are useful in providing

immunological probes for differential identification of the tissue(s) or cell type(s). For a number of disorders of the above tissues or cells, particularly of the immune system, expression of this gene at significantly higher or lower levels may be routinely detected in certain tissues or cell types (e.g. immune, cancerous and wounded tissues) or bodily fluids (e.g., lymph, serum, plasma, urine, synovial fluid and spinal fluid) or another tissue or cell sample taken from an individual having such a disorder, relative to the standard gene expression level, i.e., the expression level in healthy tissue or bodily fluid from an individual not having the disorder.

Predicted epitopes include those comprising a sequence shown in SEQ ID NO: 384 as residues: Gly-19 to Gln-28, Pro-36 to Phe-42.

The tissue distribution in tumors of colon, ovary, and breast origins indicates that the protein product of this gene is useful for the diagnosis and intervention of these tumors, in addition to other tumors where expression has been indicated. Because the gene is expressed in cells of lymphoid origin, the natural gene product may be involved in immune functions. Therefore it may also be used as an agent for immunological disorders including arthritis, asthma, immune deficiency diseases such as AIDS, and leukemia. Protein, as well as, antibodies directed against the protein may show utility as a tumor marker and/or immunotherapy targets for the above listed tumors and tissues.

Many polynucleotide sequences, such as EST sequences, are publicly available and accessible through sequence databases. Some of these sequences are related to SEQ ID NO:146 and may have been publicly available prior to conception of the present invention. Preferably, such related polynucleotides are specifically excluded from the scope of the present invention. To list every related sequence is cumbersome. Accordingly, preferably excluded from the present invention are one or more polynucleotides comprising a nucleotide sequence described by the general formula of a-b, where a is any integer between 1 to 4299 of SEQ ID NO:146, b is an integer of 15 to 4313, where both a and b correspond to the positions of nucleotide residues shown in SEQ ID NO:146, and where b is greater than or equal to a + 14.

FEATURES OF PROTEIN ENCODED BY GENE NO: 137

This gene is expressed primarily in TNF and INF induced epithelial cells, T cells and kidney.

Polynucleotides and polypeptides of the invention are useful as reagents for differential identification of the tissue(s) or cell type(s) present in a biological sample and for diagnosis of diseases and conditions which include, but are not limited to, inflammatory conditions particularly inflammatory reactions in the kidney. Similarly, polypeptides and antibodies directed to these polypeptides are useful in providing immunological probes for differential identification of the tissue(s) or cell type(s). For a number of disorders of the above tissues or cells, particularly of renal system, expression of this gene at significantly higher or lower levels may be routinely detected in certain tissues or cell types (e.g. kidney, immune, cancerous and wounded tissues) or bodily fluids (e.g., lymph, serum, plasma, urine, synovial fluid and spinal fluid) or another tissue or cell sample taken from an individual having such a disorder, relative to the standard gene expression level, i.e., the expression level in healthy tissue or bodily fluid from an individual not having the disorder.

Predicted epitopes include those comprising a sequence shown in SEQ ID NO: 385 as residues: Thr-67 to Gly-72, Gln-132 to Ala-145, Arg-150 to Pro-157.

The tissue distribution in TNF and INF induced epithelial cells indicates that the protein products of this gene are useful for treating the damage caused by inflammation of the kidney. Furthermore, the tissue distribution in kidney indicates that this gene or gene product is useful in the treatment and/or detection of kidney diseases including renal failure, nephritus, renal tubular acidosis, proteinuria, pyuria, edema, pyelonephritis, hydronephritis, nephrotic syndrome, crush syndrome, glomerulonephritis, hematuria, renal colic and kidney stones, in addition to Wilms Tumor Disease, and congenital kidney abnormalities such as horseshoe kidney, polycystic kidney, and Falconi's syndrome. Protein, as well as, antibodies directed against the protein may show utility as a tumor marker and/or immunotherapy targets for the above listed tissues.

Many polynucleotide sequences, such as EST sequences, are publicly available and accessible through sequence databases. Some of these sequences are related to SEQ ID NO:147 and may have been publicly available prior to conception

of the present invention. Preferably, such related polynucleotides are specifically excluded from the scope of the present invention. To list every related sequence is cumbersome. Accordingly, preferably excluded from the present invention are one or more polynucleotides comprising a nucleotide sequence described by the general formula of a-b, where a is any integer between 1 to 1169 of SEQ ID NO:147, b is an integer of 15 to 1183, where both a and b correspond to the positions of nucleotide residues shown in SEQ ID NO:147, and where b is greater than or equal to a + 14.

FEATURES OF PROTEIN ENCODED BY GENE NO: 138

The gene encoding the disclosed cDNA is thought to reside on chromosome 1. Accordingly, polynucleotides related to this invention are useful as a marker in linkage analysis for chromosome 1. (See Genbank Accession No. D63485).

This gene is expressed primarily in breast cancer and colon cancer, and to a lesser extent in thymus and fetal spleen.

Polynucleotides and polypeptides of the invention are useful as reagents for differential identification of the tissue(s) or cell type(s) present in a biological sample and for diagnosis of diseases and conditions which include, but are not limited to, cancers, especially of the breast and colon tissues. Similarly, polypeptides and antibodies directed to these polypeptides are useful in providing immunological probes for differential identification of the tissue(s) or cell type(s). For a number of disorders of the above tissues or cells, particularly of the immune system, expression of this gene at significantly higher or lower levels may be routinely detected in certain tissues or cell types (e.g. breast, colon, cancerous and wounded tissues) or bodily fluids (e.g., lymph, serum, plasma, urine, synovial fluid and spinal fluid) or another tissue or cell sample taken from an individual having such a disorder, relative to the standard gene expression level, i.e., the expression level in healthy tissue or bodily fluid from an individual not having the disorder.

The tissue distribution in tumors of colon and breast origins indicates that the protein product of this gene is useful for the diagnosis and intervention of these tumors, in addition to other tumors where expression has been indicated. Protein, as

well as, antibodies directed against the protein may show utility as a tumor marker and/or immunotherapy targets for the above listed tumors and tissues.

Many polynucleotide sequences, such as EST sequences, are publicly available and accessible through sequence databases. Some of these sequences are related to SEQ ID NO:148 and may have been publicly available prior to conception of the present invention. Preferably, such related polynucleotides are specifically excluded from the scope of the present invention. To list every related sequence is cumbersome. Accordingly, preferably excluded from the present invention are one or more polynucleotides comprising a nucleotide sequence described by the general formula of a-b, where a is any integer between 1 to 720 of SEQ ID NO:148, b is an integer of 15 to 734, where both a and b correspond to the positions of nucleotide residues shown in SEQ ID NO:148, and where b is greater than or equal to a + 14.

FEATURES OF PROTEIN ENCODED BY GENE NO: 139

The gene encoding the disclosed cDNA is thought to reside on chromosome 17. Accordingly, polynucleotides related to this invention are useful as a marker in linkage analysis for chromosome 17.

This gene is expressed primarily in CD34 positive cells, and to lesser extent in activated T-cells and neutrophils.

Polynucleotides and polypeptides of the invention are useful as reagents for differential identification of the tissue(s) or cell type(s) present in a biological sample and for diagnosis of diseases and conditions which include, but are not limited to, immune related diseases and hematopoietic disorders. Similarly, polypeptides and antibodies directed to these polypeptides are useful in providing immunological probes for differential identification of the tissue(s) or cell type(s). For a number of disorders of the above tissues or cells, particularly of the immune system and hematopoietic system, expression of this gene at significantly higher or lower levels may be routinely detected in certain tissues or cell types (e.g. immune, cancerous and wounded tissues) or bodily fluids (e.g., lymph, serum, plasma, urine, synovial fluid and spinal fluid) or another tissue or cell sample taken from an individual having such

a disorder, relative to the standard gene expression level, i.e., the expression level in healthy tissue or bodily fluid from an individual not having the disorder.

The tissue distribution in CD34 positive cells, T-cells and neutrophils indicates that the protein product of this gene is useful for the treatment and diagnosis of hematopoietic disorders and immune related diseases, such as anemia, leukemia, inflammation, infection, allergy, immunodeficiency disorders, arthritis, asthma, immune deficiency diseases such as AIDS. Furthermore, this gene product may be involved in the regulation of cytokine production, antigen presentation, or other processes that may also suggest a usefulness in the treatment of cancer (e.g. by boosting immune responses). Since the gene is expressed in cells of lymphoid origin, the gene or protein, as well as, antibodies directed against the protein may show utility as a tumor marker and/or immunotherapy targets for the above listed tissues. In addition, this gene product may have commercial utility in the expansion of stem cells and committed progenitors of various blood lineages, and in the differentiation and/or proliferation of various cell types. Expression of this gene product in T cells and neutrophils also strongly indicates a role for this protein in immune function and immune surveillance. Protein, as well as, antibodies directed against the protein may show utility as a tumor marker and/or immunotherapy targets for the above listed tissues.

Many polynucleotide sequences, such as EST sequences, are publicly available and accessible through sequence databases. Some of these sequences are related to SEQ ID NO:149 and may have been publicly available prior to conception of the present invention. Preferably, such related polynucleotides are specifically excluded from the scope of the present invention. To list every related sequence is cumbersome. Accordingly, preferably excluded from the present invention are one or more polynucleotides comprising a nucleotide sequence described by the general formula of a-b, where a is any integer between 1 to 1391 of SEQ ID NO:149, b is an integer of 15 to 1405, where both a and b correspond to the positions of nucleotide residues shown in SEQ ID NO:149, and where b is greater than or equal to a + 14.

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FEATURES OF PROTEIN ENCODED BY GENE NO: 140

This gene was recently published by another group, who called the gene KIAA0313 gene. (See Genbank Accession No. d1021609.)

In specific embodiments, polypeptides of the invention comprise, or alternatively consists of, an amino acid sequence selected from the group: LYATATVISSPSTEXLSQDQGDRASLDAADSGRGSWTSCSSGSHDNIQTIQHQ RSWETLPFGHTHFDYSGDPAGLWASSSHMDQIMFSDHSTKYNRQNQSRESLE QAQSRASWASSTGYWGEDSEGDTGTIKRRGGKDVSIEAESSSLTSVTTEETKP VPMPAHIAVASSTTKGLIARKEGRYREPPPTPPGYIGIPITDFPEGHSHPARKPP DYNVALQRSRMVARSSDTAGPSSVQQPHGHPTSSRPVNKPQWHKXNESDPR LAPYQSQGFSTEEDEDEQVSAV (SEQ ID NO:1012), HMDQIMFSDHSTKYNRQNQSRESLEQAQSRASWASSTGYWGE (SEQ ID NO:1013), SVTTEETKPVPMPAHIAVASSTTKGLIARKEGRYREPPPTPPGYIGIPITD (SEQ ID NO:1014), and/or VALQRSRMVARSSDTAGPSSVQQPHGHPTSSRPVNKPQWHKXNESDPRLAP YQSQGF (SEQ ID NO:1015). Moreover, fragments and variants of these polypeptides (such as, for example, fragments as described herein, polypeptides at least 80%, 85%, 90%, 95%, 96%, 97%, 98%, or 99% identical to these polypeptides and polypeptides encoded by the polynucleotide which hybridizes, under stringent conditions, to the polynucleotide encoding these polypeptides) are encompassed by the invention. Antibodies that bind polypeptides of the invention are also encompassed by the invention. Polynucleotides encoding these polypeptides are also encompassed by the invention.

The gene encoding the disclosed cDNA is thought to reside on chromosome 4. Accordingly, polynucleotides related to this invention are useful as a marker in linkage analysis for chromosome 4. (See Genbank Accession No. AB002311).

This gene is expressed primarily in ovarian cancer, tumors of the Testis, brain, and colon.

Polynucleotides and polypeptides of the invention are useful as reagents for differential identification of the tissue(s) or cell type(s) present in a biological sample

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and for diagnosis of diseases and conditions which include, but are not limited to, ovarian, testicle, brain and colon cancers. Similarly, polypeptides and antibodies directed to these polypeptides are useful in providing immunological probes for differential identification of the tissue(s) or cell type(s). For a number of disorders of the above tissues or cells, particularly of the male and female reproductive systems, expression of this gene at significantly higher or lower levels may be routinely detected in certain tissues or cell types (e.g. brain, testis, colon, ovary, cancerous and wounded tissues) or bodily fluids (e.g., lymph, serum, plasma, urine, synovial fluid and spinal fluid) or another tissue or cell sample taken from an individual having such a disorder, relative to the standard gene expression level, i.e., the expression level in healthy tissue or bodily fluid from an individual not having the disorder.

The tissue distribution in tumors of colon, ovary, testis, and brain origins indicates that the protein product of this gene is useful for the diagnosis and intervention of these tumors, in addition to other tumors where expression has been indicated. Protein, as well as, antibodies directed against the protein may show utility as a tumor marker and/or immunotherapy targets for the above listed tumors and tissues.

Many polynucleotide sequences, such as EST sequences, are publicly available and accessible through sequence databases. Some of these sequences are related to SEQ ID NO:150 and may have been publicly available prior to conception of the present invention. Preferably, such related polynucleotides are specifically excluded from the scope of the present invention. To list every related sequence is cumbersome. Accordingly, preferably excluded from the present invention are one or more polynucleotides comprising a nucleotide sequence described by the general formula of a-b, where a is any integer between 1 to 2876 of SEQ ID NO:150, b is an integer of 15 to 2890, where both a and b correspond to the positions of nucleotide residues shown in SEQ ID NO:150, and where b is greater than or equal to a + 14.

FEATURES OF PROTEIN ENCODED BY GENE NO: 141

The gene encoding the disclosed cDNA is thought to reside on chromosome 18. Accordingly, polynucleotides related to this invention are useful as a marker in linkage analysis for chromosome 18.

This gene is expressed primarily in spleen and colon cancer.

Polynucleotides and polypeptides of the invention are useful as reagents for differential identification of the tissue(s) or cell type(s) present in a biological sample and for diagnosis of diseases and conditions which include, but are not limited to, colon cancer and immunological disorders. Similarly, polypeptides and antibodies directed to these polypeptides are useful in providing immunological probes for differential identification of the tissue(s) or cell type(s). For a number of disorders of the above tissues or cells, particularly of the gastrointestinal tract and immune systems, expression of this gene at significantly higher or lower levels may be routinely detected in certain tissues or cell types (e.g. spleen, colon, cancerous and wounded tissues) or bodily fluids (e.g., lymph, serum, plasma, urine, synovial fluid and spinal fluid) or another tissue or cell sample taken from an individual having such a disorder, relative to the standard gene expression level, i.e., the expression level in healthy tissue or bodily fluid from an individual not having the disorder.

The tissue distribution in colon tumors indicates that the protein product of this gene is useful for the diagnosis and intervention of such tumors, in addition to other tissues and cell types where expression has been indicated. This gene product may be involved in the regulation of cytokine production, antigen presentation, or other processes that may also suggest a usefulness in the treatment of cancer (e.g. by boosting immune responses). Since the gene is expressed in cells of lymphoid origin, the natural gene product may be involved in immune functions. Therefore it may be also used as an agent for immunological disorders including arthritis, asthma, immunodeficiency diseases such as AIDS, leukemia, rheumatoid arthritis, granulomatous disease, inflammatory bowel disease, sepsis, acne, neutropenia, neutrophilia, psoriasis, hypersensitivities, such as T-cell mediated cytotoxicity; immune reactions to transplanted organs and tissues, such as host-versus-graft and graft-versus-host diseases, or autoimmunity disorders, such as autoimmune infertility, lens tissue injury, demyelination, systemic lupus erythematosis, drug induced hemolytic anemia, rheumatoid arthritis, Sjogren's disease, scleroderma and tissues. In

addition, this gene product may have commercial utility in the expansion of stem cells and committed progenitors of various blood lineages, and in the differentiation and/or proliferation of various cell types. Protein, as well as, antibodies directed against the protein may show utility as a tumor marker and/or immunotherapy targets for the above listed tissues. Protein, as well as, antibodies directed against the protein may show utility as a tumor marker and/or immunotherapy targets for the above listed tumors and tissues.

Many polynucleotide sequences, such as EST sequences, are publicly available and accessible through sequence databases. Some of these sequences are related to SEQ ID NO:151 and may have been publicly available prior to conception of the present invention. Preferably, such related polynucleotides are specifically excluded from the scope of the present invention. To list every related sequence is cumbersome. Accordingly, preferably excluded from the present invention are one or more polynucleotides comprising a nucleotide sequence described by the general formula of a-b, where a is any integer between 1 to 2385 of SEQ ID NO:151, b is an integer of 15 to 2399, where both a and b correspond to the positions of nucleotide residues shown in SEQ ID NO:151, and where b is greater than or equal to a + 14.

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FEATURES OF PROTEIN ENCODED BY GENE NO: 142

The translation product of this gene is homologous to a T cell translocation protein, a putative zinc finger factor (See Genbank Accession No. 340454), as well as to the G-protein coupled receptor TM5 consensus polypeptide (See Genbank Accession No. R50734).

In specific embodiments, polypeptides of the invention comprise, or alternatively consists of, an amino acid sequence selected from the group: CLLFVFVSLGMRCLFWTIVYNVLYLKHKCNTVLLCYHLCSI (SEQ ID NO:1016), and/or ACSKLIPAFEMVMRAKDNVYHLDCFACQLCNQRXCVGDKFFLKNNXXLCQ TDYEEGLMKEGYAPXVR (SEQ ID NO:1017). Moreover, fragments and variants of these polypeptides (such as, for example, fragments as described herein,

polypeptides at least 80%, 85%, 90%, 95%, 96%, 97%, 98%, or 99% identical to these polypeptides and polypeptides encoded by the polynucleotide which hybridizes, under stringent conditions, to the polynucleotide encoding these polypeptides) are encompassed by the invention. Antibodies that bind polypeptides of the invention are also encompassed by the invention. Polynucleotides encoding these polypeptides are also encompassed by the invention.

This gene is expressed primarily in fetal brain, and to a lesser extent in frontal cortex.

Polynucleotides and polypeptides of the invention are useful as reagents for differential identification of the tissue(s) or cell type(s) present in a biological sample and for diagnosis of diseases and conditions which include, but are not limited to, neurological disorders, including brain cancer. Similarly, polypeptides and antibodies directed to these polypeptides are useful in providing immunological probes for differential identification of the tissue(s) or cell type(s). For a number of disorders of the above tissues or cells, particularly of the Central Nervous System, expression of this gene at significantly higher or lower levels may be routinely detected in certain tissues or cell types (e.g. brain, cancerous and wounded tissues) or bodily fluids (e.g., lymph, serum, plasma, urine, synovial fluid and spinal fluid) or another tissue or cell sample taken from an individual having such a disorder, relative to the standard gene expression level, i.e., the expression level in healthy tissue or bodily fluid from an individual not having the disorder.

The tissue distribution in fetal brain indicates that the protein product of this gene is useful for the detection/treatment of neurodegenerative disease states and behavioral disorders such as Alzheimer's Disease, Parkinson's Disease, Huntington's Disease, schizophrenia, mania, dementia, paranoia, obsessive compulsive disorder and panic disorder. In addition, the gene or gene product may also play a role in the treatment and/or detection of developmental disorders associated with the developing embryo. Furthermore, elevated expression of this gene product within the frontal cortex of the brain indicates that it may be involved in neuronal survival; synapse formation; conductance; neural differentiation, etc. Such involvement may impact many processes, such as learning and cognition. It may also be useful in the treatment of such neurodegenerative disorders as schizophrenia; ALS; or Alzheimer's.

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Protein, as well as, antibodies directed against the protein may show utility as a tissue-specific marker and/or immunotherapy target for the above listed tissues.

Many polynucleotide sequences, such as EST sequences, are publicly available and accessible through sequence databases. Some of these sequences are related to SEQ ID NO:152 and may have been publicly available prior to conception of the present invention. Preferably, such related polynucleotides are specifically excluded from the scope of the present invention. To list every related sequence is cumbersome. Accordingly, preferably excluded from the present invention are one or more polynucleotides comprising a nucleotide sequence described by the general formula of a-b, where a is any integer between 1 to 788 of SEQ ID NO:152, b is an integer of 15 to 802, where both a and b correspond to the positions of nucleotide residues shown in SEQ ID NO:152, and where b is greater than or equal to a + 14.

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FEATURES OF PROTEIN ENCODED BY GENE NO: 143

The translation product of this gene has significant homology to the Fas ligand, which is a cysteine-rich type II transmembrane protein/tumor necrosis factor receptor homolog. Mutations within this protein have been shown to result in generalized lymphoproliferative diseases leading to the development of lymphadenopathy and autoimmune disease (See Medline Article No. 94185175).

In specific embodiments, polypeptides of the invention comprise, or alternatively consists of, the following amino acid sequence: SALSEPGAPDRRRPCPESVPRRPDDEQWPPPTALCLDVAPLPPSS (SEQ ID NO:1018). Moreover, fragments and variants of this polypeptide (such as, for example, fragments as described herein, polypeptides at least 80%, 85%, 90%, 95%, 96%, 97%, 98%, or 99% identical to these polypeptides and polypeptides encoded by the polynucleotide which hybridize, under stringent conditions, to the polynucleotide encoding this polypeptide are encompassed by the invention. Antibodies that bind polypeptides of the invention are also encompassed by the invention. Polynucleotides encoding this polypeptide are also encompassed by the invention. (See Genbank Accession No. 473565).

This gene is expressed primarily in osteoblasts, lung, and brain.

Polynucleotides and polypeptides of the invention are useful as reagents for differential identification of the tissue(s) or cell type(s) present in a biological sample and for diagnosis of diseases and conditions which include, but are not limited to, osteoblast-related, pulmonary, neurological, and immunological diseases. Similarly, polypeptides and antibodies directed to these polypeptides are useful in providing immunological probes for differential identification of the tissue(s) or cell type(s). For a number of disorders of the above tissues or cells, particularly of the skeletal and nervous systems, expression of this gene at significantly higher or lower levels may be routinely detected in certain tissues or cell types (e.g. lung, brain, skeletal, cancerous and wounded tissues) or bodily fluids (e.g., lymph, serum, plasma, urine, synovial fluid and spinal fluid) or another tissue or cell sample taken from an individual having such a disorder, relative to the standard gene expression level, i.e., the expression level in healthy tissue or bodily fluid from an individual not having the disorder.

Predicted epitopes include those comprising a sequence shown in SEQ ID NO: 391 as residues: Trp-33 to Thr-40, Lys-45 to Ile-63.

The tissue distribution in osteoblasts, lung, and brain, combined with its homology to the Fas ligand, indicates that the protein product of this gene is useful for the diagnosis and intervention of these tumors, in addition to other tumors where expression has been indicated. Protein, as well as, antibodies directed against the protein may show utility as a tumor marker and/or immunotherapy targets for the above listed tumors and tissues. Because the Fas ligand gene is known to be expressed in cells of lymphoid origin, the natural gene product may be involved in immune functions. Therefore it may be also used as an agent for immunological disorders including asthma, immune deficiency diseases such as AIDS and leukemia, and various autoimmune disorders including lupus and arthritis. Protein, as well as, antibodies directed against the protein may show utility as a tissue-specific marker and/or immunotherapy target for the above listed tissues.

Many polynucleotide sequences, such as EST sequences, are publicly available and accessible through sequence databases. Some of these sequences are related to SEQ ID NO:153 and may have been publicly available prior to conception

Docket No. 2000.09

of the present invention. Preferably, such related polynucleotides are specifically excluded from the scope of the present invention. To list every related sequence is cumbersome. Accordingly, preferably excluded from the present invention are one or more polynucleotides comprising a nucleotide sequence described by the general formula of a-b, where a is any integer between 1 to 447 of SEQ ID NO:153, b is an integer of 15 to 461, where both a and b correspond to the positions of nucleotide residues shown in SEQ ID NO:153, and where b is greater than or equal to a + 14.

FEATURES OF PROTEIN ENCODED BY GENE NO: 144

This gene shares sequence homology with a 21.5 KD transmembrane protein in the SEC15-SAP4 intergenic region of yeast. (See Genbank Accession No. 1723971.)

In specific embodiments, polypeptides of the invention comprise, or alternatively consists of, an amino acid sequence selected from the group: PVGYLDKQVPDTSVQETDRILVEKRCWDIALGPLKQIPMNLFI (SEQ ID NO:1019), AHASESGERWWACCGVRFGLRSIEAIGRSCCHDGPGGLVANRGRRFKWAIEL SGPGGGSRGRSDRGSGQGDSLYPVGYLDKQVPDTSVQETDRILVEKRCWDIA LGPLKQIPMNLFIMYMAGNTISIFPTMMVCMMAWRPIQALMAISATFKMLES SSQKFLQGLVYLIGNLMGLALAVYKCQSMGLLPTHASDWLAFIEPPERMEFS GGGLLL (SEQ ID NO:1020), PVGYLDKQVPDTSVQETDRILVEKRCW DIALGPLKQIPMNLFI (SEQ ID NO:1022), and/or ATFKMLESSSQKFLQGLVYLIGNLMGLALAVYKCQSMGLLPTHASD (SEQ ID NO:1021). Moreover, fragments and variants of these polypeptides (such as, for example, fragments as described herein, polypeptides at least 80%, 85%, 90%, 95%, 96%, 97%, 98%, or 99% identical to these polypeptides and polypeptides encoded by the polynucleotide which hybridizes, under stringent conditions, to the polynucleotide encoding these polypeptides) are encompassed by the invention. Antibodies that bind polypeptides of the invention are also encompassed by the invention. Polynucleotides encoding these polypeptides are also encompassed by the invention.

Docket No. 2000.2.0

This gene is expressed primarily in osteoclastoma, hemangiopericytoma, liver, lung.

Polynucleotides and polypeptides of the invention are useful as reagents for differential identification of the tissue(s) or cell type(s) present in a biological sample and for diagnosis of diseases and conditions which include, but are not limited to, osteoclastoma, hemangiopericytoma, liver and lung tumors. Similarly, polypeptides and antibodies directed to these polypeptides are useful in providing immunological probes for differential identification of the above tissue(s) or cell type(s). For a number of disorders of the above tissues or cells, particularly of the lung and liver systems, expression of this gene at significantly higher or lower levels may be routinely detected in certain tissues or cell types (e.g. lung, liver, cancerous and wounded tissues) or bodily fluids (e.g., lymph, serum, plasma, urine, synovial fluid and spinal fluid) or another tissue or cell sample taken from an individual having such a disorder, relative to the standard gene expression level, i.e., the expression level in healthy tissue or bodily fluid from an individual not having the disorder.

The tissue distribution indicates that the protein product of this gene is useful for the diagnosis and/or treatment of tumors of the osteoclastoma, hemangiopericytoma, liver and lung, in addition to other tumors where expression has been indicated. Protein, as well as, antibodies directed against the protein may show utility as a tissue-specific marker and/or immunotherapy target for the above listed tissues.

Many polynucleotide sequences, such as EST sequences, are publicly available and accessible through sequence databases. Some of these sequences are related to SEQ ID NO:154 and may have been publicly available prior to conception of the present invention. Preferably, such related polynucleotides are specifically excluded from the scope of the present invention. To list every related sequence is cumbersome. Accordingly, preferably excluded from the present invention are one or more polynucleotides comprising a nucleotide sequence described by the general formula of a-b, where a is any integer between 1 to 2374 of SEQ ID NO:154, b is an integer of 15 to 2388, where both a and b correspond to the positions of nucleotide residues shown in SEQ ID NO:154, and where b is greater than or equal to a + 14.

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FEATURES OF PROTEIN ENCODED BY GENE NO: 145

The translation product of this gene shares homology with the glucagon-69 gene which may indicate this gene plays a role in regulating metabolism. (See Genbank Accession No. A60318)

In specific embodiments, polypeptides of the invention comprise, or alternatively consists of, an amino acid sequence selected from the group: PTTKLDIMEKKKHIQIRFPSFYHKLVDSGRMRSKRETRREDSDTKHNL (SEQ ID NO:1023), FLWKSLLLRYFKMRQH (SEQ ID NO:1024), and/or YHYLLSSFLSYSSSSQNLPVYGRKMGTLFECVFFFP (SEQ ID NO:1025). Moreover, fragments and variants of these polypeptides (such as, for example, fragments as described herein, polypeptides at least 80%, 85%, 90%, 95%, 96%, 97%, 98%, or 99% identical to these polypeptides and polypeptides encoded by the polynucleotide which hybridizes, under stringent conditions, to the polynucleotide encoding these polypeptides) are encompassed by the invention. Antibodies that bind polypeptides of the invention are also encompassed by the invention. Polynucleotides encoding these polypeptides are also encompassed by the invention.

This gene is expressed primarily in brain, kidney, colon, and testis.

Polynucleotides and polypeptides of the invention are useful as reagents for differential identification of the tissue(s) or cell type(s) present in a biological sample and for diagnosis of diseases and conditions which include, but are not limited to, brain, kidney, colon, and testicular cancer. Similarly, polypeptides and antibodies directed to these polypeptides are useful in providing immunological probes for differential identification of the tissue(s) or cell type(s). For a number of disorders of the above tissues or cells, particularly of the male reproductive system, neurological, circulatory, and gastrointestinal systems, expression of this gene at significantly higher or lower levels may be routinely detected in certain tissues or cell types (e.g. brain, kidney, colon, testis, cancerous and wounded tissues) or bodily fluids (e.g., lymph, serum, plasma, urine, synovial fluid and spinal fluid) or another tissue or cell sample taken from an individual having such a disorder, relative to the standard gene

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expression level, i.e., the expression level in healthy tissue or bodily fluid from an individual not having the disorder.

The tissue distribution in brain, kidney, colon, and testis origins, indicates that the protein product of this gene is useful for the diagnosis and intervention of tumors of these tissues. The protein product of this gene is useful for the detection/treatment of neurodegenerative disease states, behavioral disorders, or inflammatory conditions such as Alzheimer's Disease, Parkinson's Disease, Huntington's Disease, Tourette's Syndrome, meningitis, encephalitis, demyelinating diseases, peripheral neuropathies, neoplasia, trauma, congenital malformations, spinal cord injuries, ischemia and infarction, aneurysms, hemorrhages, schizophrenia, mania, dementia, paranoia, obsessive compulsive disorder, panic disorder, learning disabilities, ALS, psychoses , autism, and altered behaviors, including disorders in feeding, sleep patterns, balance, and perception. In addition, elevated expression of this gene product in regions of the brain indicates that it plays a role in normal neural function. Potentially, this gene product is involved in synapse formation, neurotransmission, learning, cognition, homeostasis, or neuronal differentiation or survival. Moreover, the gene or gene product may also play a role in the treatment and/or detection of developmental disorders associated with the developing embryo, sexually-linked disorders, or disorders of the cardiovascular system. Protein, as well as, antibodies directed against the protein may show utility as a tumor marker and/or immunotherapy targets for the above listed tissues. Protein, as well as, antibodies directed against the protein may show utility as a tumor marker and/or immunotherapy targets for the above listed tumors and tissues. The tissue distribution indicates that the protein product of this gene is useful for the detection/treatment of neurodegenerative disease states and behavioral disorders such as Alzheimer's Disease, Parkinson's Disease, Huntington's Disease, schizophrenia, mania, dementia, paranoia, obsessive compulsive disorder and panic disorder. In addition, the gene or gene product may also play a role in the treatment and/or detection of developmental disorders associated with the developing embryo, sexually-linked disorders, or disorders of the cardiovascular system.

Many polynucleotide sequences, such as EST sequences, are publicly available and accessible through sequence databases. Some of these sequences are related to SEQ ID NO:155 and may have been publicly available prior to conception

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of the present invention. Preferably, such related polynucleotides are specifically excluded from the scope of the present invention. To list every related sequence is cumbersome. Accordingly, preferably excluded from the present invention are one or more polynucleotides comprising a nucleotide sequence described by the general formula of a-b, where a is any integer between 1 to 628 of SEQ ID NO:155, b is an integer of 15 to 642, where both a and b correspond to the positions of nucleotide residues shown in SEQ ID NO:155, and where b is greater than or equal to a + 14.

FEATURES OF PROTEIN ENCODED BY GENE NO: 146

The translation product of this gene shares sequence homology with goliath protein, which is a Drosophila protein thought to be important in the regulation of gene expression during development. Protein may serve as a transcription factor.

In specific embodiments, polypeptides of the invention comprise, or alternatively consists of, an amino acid sequence selected from the group:
TEHIIAVMITELRGKDILSYLEKNISVQMTIAVGTRMPPKNFSRGSLVFVSISFI
VLMIISSAWLIFYFIQKIRYTNARDRNQRRLGDAAKKAISKLTTRTVKKGDKE
TDPDFDHCAVCIESYKQNDVVRILPCKHVFHKSCVDPWLSEHCTCPMCKLNI
LKALGIV (SEQ ID NO:1026),
MTHPGTEHIIAVMITELRGKDILSYLEKNISVQMTIAVGTRMPPKNFSRGSLVF
VSISFIVLMIISSAWLIFYFIQKIRYTNARDRNQRRLGDAAKKAISKLTTRTVKK
GDKETDPDFDHCAVCIESYKQNDVVRILPCKHVFHKSCVDPWLSEHCTCPMC
KLNILKALGIVPNLPCTDNVAFDMERLTRTQAVNRRSALGDLAGDNSLGLEP
LRTSGISPLPQDGELTPRTGEINIAVTKEWFIIASFGLLSALTLCYMIIRATASLN
ANEVEWF (SEQ ID NO:1027),
TEHIIAVMITELRGKDILSYLEKNISVQMTIAVGTRMPPKNFSRGSLVFVSISFI
VLMIISSAWLIFYF (SEQ ID NO:1028),
SISFIVLMIISSAWLIFYFIQKIRYTNARDRNQRRLGDAAKKAISKLTTRTVKKG
DKE (SEQ ID NO:1029),
VKKGDKETDPDFDHCAVCIESYKQNDVVRILPCKHVFHKSCVDPWLSEHCTC
PMCKLNILKALGIV (SEQ ID NO:1030),

MTHPGTEHIIAVMITELRGKDILSYLEKNISVQMTI
AVGTRMPPKNFSRGSLVFVSISFIVLMIISSAWLIFYFIQKIRYTNARDRNQRRL
GDAAKKAISKLTTRT (SEQ ID NO:1031),
AAKKAISKLTTRTVKKGDKETDPDFDHCAVCIESYKQNDVVRILPCKHVFHK
SCVDPWLSEHCTCPMCKLNILKALGIVPNLPC (SEQ ID NO:1032),
TQAVNRRSALGDLAGDNSLGLEPLRTSGISPLPQDGELTPRTGEINIAVTKEWF
IIASFGLLSALTLCYMIIRATASLNANEVEWF (SEQ ID NO:1033),
PLHGVADHLGCDPQTRFFVPPNIKQWIALLQRGNCTFKEKISRAAFHNAVAV
VIYNNKSKEEPVTMTHPGTEHIIAVMITELRGKDILSYLEKNISVQMTIAVGTR
MPPKNFSRGSLVFVSISFIVLMIISSAWLIFYFIQKIRYTNARDRNQRRLGDAAK
KAISKLTTRTVKKGDKETDPDFDHCAVCIESYKQNDVVRILPCKHVFHKSCV
DPWLSEHCTCPMCKLNILKALGIVPNLPCTDNVAFDMERLTRTQAVNRRSAL
GDLAGDNSLGLEPLRTSGISPLPQDGELTPRTGEINIAVTKEWFIIASFGLLSAL
TLCYMIIRATASLNANEVEWF (SEQ ID NO:1034), and/or
HGVADHLGCDPQTRFFVPPNIKQWIALLQRGNCTFKEKISRAAFHNAVAVVI
YNNKSKEE (SEQ ID NO:1035). Moreover, fragments and variants of these polypeptides (such as, for example, fragments as described herein, polypeptides at least 80%, 85%, 90%, 95%, 96%, 97%, 98%, or 99% identical to these polypeptides and polypeptides encoded by the polynucleotide which hybridizes, under stringent conditions, to the polynucleotide encoding these polypeptides) are encompassed by the invention. Antibodies that bind polypeptides of the invention are also encompassed by the invention. Polynucleotides encoding these polypeptides are also encompassed by the invention. (See Genbank Accession No. 157535).

When tested against Jurkat cell lines, supernatants removed from cells containing this gene activated the GAS assay. Thus, it is likely that this gene activates T-cells through the Jak-STAT signal transduction pathway. The gamma activating sequence (GAS) is a promoter element found upstream of many genes which are involved in the Jak-STAT pathway. The Jak-STAT pathway is a large, signal transduction pathway involved in the differentiation and proliferation of cells. Therefore, activation of the Jak-STAT pathway, reflected by the binding of the GAS element, can be used to indicate proteins involved in the proliferation and differentiation of cells.

This gene is expressed primarily in macrophage, breast, kidney and to a lesser extent in synovium, hypothalamus and rhabdomyosarcoma.

Polynucleotides and polypeptides of the invention are useful as reagents for differential identification of the tissue(s) or cell type(s) present in a biological sample and for diagnosis of diseases and conditions which include, but are not limited to, schizophrenia and cancer. Similarly, polypeptides and antibodies directed to these polypeptides are useful in providing immunological probes for differential identification of the tissue(s) or cell type(s). For a number of disorders of the above tissues or cells, particularly of the immune and neural system, expression of this gene at significantly higher or lower levels may be routinely detected in certain tissues or cell types (e.g. brain, kidney, immune, cancerous and wounded tissues) or bodily fluids (e.g., lymph, serum, plasma, urine, synovial fluid and spinal fluid) or another tissue or cell sample taken from an individual having such a disorder, relative to the standard gene expression level, i.e., the expression level in healthy tissue or bodily fluid from an individual not having the disorder.

The tissue distribution in macrophage, hypothalamus, and kidney, combined with the homology to a zinc finger protein indicates that the protein product of this gene is useful for the treatment of schizophrenia, kidney disease and other cancers. Furthermore, the tissue distribution in macrophage, breast, and kidney origins indicates that the protein product of this gene is useful for the diagnosis and intervention of tumors within these tissues, in addition to other tumors where expression has been indicated. Protein, as well as, antibodies directed against the protein may show utility as a tumor marker and/or immunotherapy targets for the above listed tumors and tissues. Because the gene is expressed in cells of lymphoid origin, the natural gene product may be involved in immune functions. Therefore it may be also used as an agent for immunological disorders including arthritis, asthma, immune deficiency diseases such as AIDS, and leukemia.

Many polynucleotide sequences, such as EST sequences, are publicly available and accessible through sequence databases. Some of these sequences are related to SEQ ID NO:156 and may have been publicly available prior to conception of the present invention. Preferably, such related polynucleotides are specifically excluded from the scope of the present invention. To list every related sequence is

cumbersome. Accordingly, preferably excluded from the present invention are one or more polynucleotides comprising a nucleotide sequence described by the general formula of a-b, where a is any integer between 1 to 1237 of SEQ ID NO:156, b is an integer of 15 to 1251, where both a and b correspond to the positions of nucleotide residues shown in SEQ ID NO:156, and where b is greater than or equal to a + 14.

FEATURES OF PROTEIN ENCODED BY GENE NO: 147

The translation product of this gene shares sequence homology with HNP36 protein, an equilibrative nucleoside transporter, which is thought to be important in gene transcription as well as serving as an important component of the nucleoside transport apparatus (See Genbank Accession No. 1845345).

In specific embodiments, polypeptides of the invention comprise, or alternatively consists of, an amino acid sequence selected from the group:

MSGQGLAGFFASVAMICAIASGSELSESAFGYFITACAVIILTIICYLGLP RLEFYRYYQQLKLEGPGEQETKLDLISKGEEPRAGKEESGVSVSNSQPTNESH SIKAILKNISVLAFSVCFIFTITIGMFPAVTVEVKSSIAGSSTWERYFIPVSCFLTF NIFDWLGRSLTAVFMWPGKDSRWLPSWXLARLVFVPLLLLCNIKPRRYLTVV FEHDAWFIFFMAAFAFSNGYLASLCMCFGPKKVKPAEAETAEPSWPSSCVW VWHWGLFSPSCSGQLCDKGWTEGLPASLPVCLLPLPSARGDPEWSGGFFF(SE Q ID NO:1036),

MSGQGLAGFFASVAMICAIASGSELSESAFGYFITACAVIILTIICYLGLPRLEF YRYYQQLKLEGPGEQETKLDLISKGEEPRAGKEESGVSVSNSQPTNESHSI (SEQ ID NO:1037),

SGVSVSNSQPTNESHSIKAILKNISVLAFSVCFIFTITIGMFPAVTVEVKSSIAGS STWERYFIPVSCFLTFNIFDWLGRS (SEQ ID NO:1038),

TIGMFPAVTVEVKSSIAGSSTWERYFIPVSCFLTFNIFDWLGRSLTAVFMWPG KDSRWLPSWXLARLVFVPLLLLCNIKPRRYLTVVFEHDA (SEQ ID NO:1039), and/or

FGPKKVKPAEAETAEPSWPSSCVWVWHWGLFSPSCSGQLCDKGWTEGLPAS LPVCLLPLPSARGDPEWSGGFFF (SEQ ID NO:1040). Moreover, fragments and

variants of these polypeptides (such as, for example, fragments as described herein, polypeptides at least 80%, 85%, 90%, 95%, 96%, 97%, 98%, or 99% identical to these polypeptides and polypeptides encoded by the polynucleotide which hybridizes, under stringent conditions, to the polynucleotide encoding these polypeptides) are encompassed by the invention. Antibodies that bind polypeptides of the invention are also encompassed by the invention. Polynucleotides encoding these polypeptides are also encompassed by the invention.

An additional embodiment is the polynucleotide fragments encoding these polypeptide fragments. The gene encoding the disclosed cDNA is thought to reside on chromosome 6. Accordingly, polynucleotides related to this invention are useful as a marker in linkage analysis for chromosome 6.

This gene is expressed primarily in eosinophils and aortic endothelium, and to a lesser extent in umbilical vein endothelial cell and thymus.

Polynucleotides and polypeptides of the invention are useful as reagents for differential identification of the tissue(s) or cell type(s) present in a biological sample and for diagnosis of diseases and conditions which include, but are not limited to, hemopoietic disease. Similarly, polypeptides and antibodies directed to these polypeptides are useful in providing immunological probes for differential identification of the tissue(s) or cell type(s). For a number of disorders of the above tissues or cells, particularly of the circulatory system, expression of this gene at significantly higher or lower levels may be routinely detected in certain tissues or cell types (e.g. circulatory, immune, cancerous and wounded tissues) or bodily fluids (e.g., lymph, serum, plasma, urine, synovial fluid and spinal fluid) or another tissue or cell sample taken from an individual having such a disorder, relative to the standard gene expression level, i.e., the expression level in healthy tissue or bodily fluid from an individual not having the disorder.

The tissue distribution eosinophils and aortic endothelium, combined with the homology to the HNP36 protein indicates that the protein product of this gene is useful for the treatment of blood neoplasias and other hemopoietic disease. Furthermore, elevated expression of this gene product by endothelial cells indicates that it may play vital roles in the regulation of endothelial cell function; secretion; proliferation; or angiogenesis. Protein, as well as, antibodies directed against the

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protein may show utility as a tumor marker and/or immunotherapy targets for the above listed tissues.

Many polynucleotide sequences, such as EST sequences, are publicly available and accessible through sequence databases. Some of these sequences are related to SEQ ID NO:157 and may have been publicly available prior to conception of the present invention. Preferably, such related polynucleotides are specifically excluded from the scope of the present invention. To list every related sequence is cumbersome. Accordingly, preferably excluded from the present invention are one or more polynucleotides comprising a nucleotide sequence described by the general formula of a-b, where a is any integer between 1 to 2113 of SEQ ID NO:157, b is an integer of 15 to 2127, where both a and b correspond to the positions of nucleotide residues shown in SEQ ID NO:157, and where b is greater than or equal to a + 14.

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FEATURES OF PROTEIN ENCODED BY GENE NO: 148

The gene encoding the disclosed cDNA is thought to reside on chromosome 5. Accordingly, polynucleotides related to this invention are useful as a marker in linkage analysis for chromosome 5.

This gene is expressed primarily in breast cancer cell lines, thymus stromal cells, and ovary.

Polynucleotides and polypeptides of the invention are useful as reagents for differential identification of the tissue(s) or cell type(s) present in a biological sample and for diagnosis of diseases and conditions which include, but are not limited to, endocrine and female reproductive system diseases including breast cancer. Similarly, polypeptides and antibodies directed to these polypeptides are useful in providing immunological probes for differential identification of the tissue(s) or cell type(s). For a number of disorders of the above tissues or cells, particularly of the endocrine system, expression of this gene at significantly higher or lower levels may be routinely detected in certain tissues or cell types (e.g. thymus, ovary, cancerous and wounded tissues) or bodily fluids (e.g., lymph, serum, plasma, urine, synovial fluid and spinal fluid) or another tissue or cell sample taken from an individual having

such a disorder, relative to the standard gene expression level, i.e., the expression level in healthy tissue or bodily fluid from an individual not having the disorder.

The tissue distribution in breast cancer cells and ovary indicates that the protein product of this gene is useful for the diagnosis and treatment of endocrine disorders. In addition, the tissue distribution in tumors of thymus, ovary, and breast origins indicates that the protein product of this gene is useful for diagnosis and intervention of these tumors, in addition to other tumors where expression has been indicated. Protein, as well as, antibodies directed against the protein may show utility as a tumor marker and/or immunotherapy targets for the above listed tumors and tissues

Many polynucleotide sequences, such as EST sequences, are publicly available and accessible through sequence databases. Some of these sequences are related to SEQ ID NO:158 and may have been publicly available prior to conception of the present invention. Preferably, such related polynucleotides are specifically excluded from the scope of the present invention. To list every related sequence is cumbersome. Accordingly, preferably excluded from the present invention are one or more polynucleotides comprising a nucleotide sequence described by the general formula of a-b, where a is any integer between 1 to 1611 of SEQ ID NO:158, b is an integer of 15 to 1625, where both a and b correspond to the positions of nucleotide residues shown in SEQ ID NO:158, and where b is greater than or equal to a + 14.

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FEATURES OF PROTEIN ENCODED BY GENE NO: 149

The translation product of this gene has homology to pmt1 and pmt 2, two conserved Schizosaccharomyces pombe genes.

In specific embodiments, polypeptides of the invention comprise, or alternatively consists of, an amino acid sequence selected from the group: DDDGFEIVPIEDPAKHRILDPEGLALGAVIASSKKAKRDLIDNSFNRYTFNEDE GELPEWFVQEEKQHRIRQLPVGKKEVEHYRKRWREINARPIXXXXXXXXXX XXXXXXXLEQTRKKAEAVVNTVDIXRTRES (SEQ ID NO:1041), DDDG FEIVPIEDPAKHRILDPEGLALGAVIASSKKAKRDLIDNSFNRYTF (SEQ ID

NO:1042), and/or KRWREINARPIXXXXXXXXXXXXXXXXXXLEQTRKKAEAVVNTVDIXRTRES (SEQ ID NO:1043). Moreover, fragments and variants of these polypeptides (such as, for example, fragments as described herein, polypeptides at least 80%, 85%, 90%, 95%, 96%, 97%, 98%, or 99% identical to these polypeptides and polypeptides encoded by the polynucleotide which hybridizes, under stringent conditions, to the polynucleotide encoding these polypeptides) are encompassed by the invention. Antibodies that bind polypeptides of the invention are also encompassed by the invention. Polynucleotides encoding these polypeptides are also encompassed by the invention. (See Genbank Accession No. e1216734).

This gene is expressed primarily in retina and ovary, and to a lesser extent in breast cancer cells, epididymus and osteosarcoma.

Polynucleotides and polypeptides of the invention are useful as reagents for differential identification of the tissue(s) or cell type(s) present in a biological sample and for diagnosis of diseases and conditions which include, but are not limited to, neuronal growth disorders, cancer and reproductive system disorders. Similarly, polypeptides and antibodies directed to these polypeptides are useful in providing immunological probes for differential identification of the tissue(s) or cell type(s). For a number of disorders of the above tissues or cells, particularly of the neural and reproductive system, expression of this gene at significantly higher or lower levels may be routinely detected in certain tissues or cell types (e.g. retina, ovary, reproductive, cancerous and wounded tissues) or bodily fluids (e.g., lymph, serum, plasma, urine, synovial fluid and spinal fluid) or another tissue or cell sample taken from an individual having such a disorder, relative to the standard gene expression level, i.e., the expression level in healthy tissue or bodily fluid from an individual not having the disorder.

Predicted epitopes include those comprising a sequence shown in SEQ ID NO: 397 as residues: Met-1 to Gly-7.

The tissue distribution in ovary, breast cancer cells, and epididymus indicates that the protein product of this gene is useful for the diagnosis or treatment of reproductive system diseases and cancers, in addition to other tumors where expression has been indicated. Protein, as well as, antibodies directed against the

protein may show utility as a tissue-specific marker and/or immunotherapy target for the above listed tissues.

Many polynucleotide sequences, such as EST sequences, are publicly available and accessible through sequence databases. Some of these sequences are related to SEQ ID NO:159 and may have been publicly available prior to conception of the present invention. Preferably, such related polynucleotides are specifically excluded from the scope of the present invention. To list every related sequence is cumbersome. Accordingly, preferably excluded from the present invention are one or more polynucleotides comprising a nucleotide sequence described by the general formula of a-b, where a is any integer between 1 to 1673 of SEQ ID NO:159, b is an integer of 15 to 1687, where both a and b correspond to the positions of nucleotide residues shown in SEQ ID NO:159, and where b is greater than or equal to a + 14.

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FEATURES OF PROTEIN ENCODED BY GENE NO: 150

In specific embodiments, polypeptides of the invention comprise, or alternatively consists of, an amino acid sequence selected from the group:
MIKDKGRARTALTSSQPAHLCPENPLLHLKAAVKEKKRNKKKKTIGSPKRIQS
PLNNKLLNSPAKTLPGACGSPQKLIDGFLKHEGPPAEKPLEELSASTSGVPGLS
SLQSDPAGCVRPPAPNLAGAVEFNDVKTLLREWITTISDPMEEDILQVVKYCT
DLIEEKDLEKLDLVIKYMKRLMQQSVESVWNMAFDFILDNVQVVLQQTYGS
TLKVT (SEQ ID NO:1044),
MIKDKGRARTALTSSQPAHLCPENPLLHLKAAVKEKKRNKKKKTIGSPKRIQ
(SEQ ID NO:1045),
KRIQSPLNNKLLNSPAKTLPGACGSPQKLIDGFLKHEGPPAEKPLEELSASTSG
VPGLSSLQSDPAGCVRPPAPNLAGAVEFNDVKTLLREWITTI SDPM (SEQ ID
NO:1046),
TISDPMEEDILQVVKYCTDLIEEKDLEKLDLVIKYMKRLMQQSVESVWNMAF
DFILDNVQVVLQQTYGSTLKVT (SEQ ID NO:1047),
VCCKTTWTLSRIKSNAIFQTDSTDCCISLFMYFITRSSFSKSFSSIRSVQYFTTW
RMSSSIGSEIVVIHSLSKVFTSLNSTAPARLGAGGLTQPAGSDCKLERPGTPEV

EAESSSRGFSAGGPSCFRNPSINFWGLPQAPGRVFAGLLSSLLFKGL (SEQ ID NO:1048), WTLSRIKSNAIFQTDSTDCCISLFM (SEQ ID NO:1049), FTTWRMSSSIGSEIVVIHSLSKVFTSLNSTAPARLGA (SEQ ID NO:1050), and/or GGPSCFRNPSINFWGLPQAPGRVFAGLL (SEQ ID NO:1051). Moreover, fragments and variants of these polypeptides (such as, for example, fragments as described herein, polypeptides at least 80%, 85%, 90%, 95%, 96%, 97%, 98%, or 99% identical to these polypeptides and polypeptides encoded by the polynucleotide which hybridizes, under stringent conditions, to the polynucleotide encoding these polypeptides) are encompassed by the invention. Antibodies that bind polypeptides of the invention are also encompassed by the invention. Polynucleotides encoding these polypeptides are also encompassed by the invention.

The gene encoding the disclosed cDNA is believed to reside on chromosome 2. Accordingly, polynucleotides related to this invention are useful as a marker in linkage analysis for chromosome 2.

This gene is expressed primarily in 12 week embryo, and to a lesser extent, in hemangiopericytoma and frontal cortex.

Polynucleotides and polypeptides of the invention are useful as reagents for differential identification of the tissue(s) or cell type(s) present in a biological sample and for diagnosis of diseases and conditions which include, but are not limited to, developmental or neural disorders, particularly hemangiopericytoma, and other proliferative conditions, including cancers. Similarly, polypeptides and antibodies directed to these polypeptides are useful in providing immunological probes for differential identification of the tissue(s) or cell type(s). For a number of disorders of the above tissues or cells, particularly of the neural system and developing systems, expression of this gene at significantly higher or lower levels may be routinely detected in certain tissues or cell types (e.g., developmental, neural, and cancerous and wounded tissues) or bodily fluids (e.g., lymph, amniotic fluid, serum, plasma, urine, synovial fluid and spinal fluid) or another tissue or cell sample taken from an individual having such a disorder, relative to the standard gene expression level, i.e., the expression level in healthy tissue or bodily fluid from an individual not having the disorder.

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Predicted epitopes include those comprising a sequence shown in SEQ ID NO: 398 as residues: Leu-4 to Lys-11.

The tissue distribution in embryonic and neural tissues indicates that the protein product of this gene is useful for the treatment of growth disorders, hemangiopericytoma and other soft tissue tumors. Moreover, the protein product of this gene is useful for the detection/treatment of neurodegenerative disease states, behavioral disorders, or inflammatory conditions such as Alzheimer's Disease, Parkinson's Disease, Huntington's Disease, Tourette's Syndrome, meningitis, encephalitis, demyelinating diseases, peripheral neuropathies, neoplasia, trauma, congenital malformations, spinal cord injuries, ischemia and infarction, aneurysms, hemorrhages, schizophrenia, mania, dementia, paranoia, obsessive compulsive disorder, panic disorder, learning disabilities, ALS, psychoses, autism, and altered behaviors, including disorders in feeding, sleep patterns, balance, and perception. In addition, elevated expression of this gene product in regions of the brain indicates that it plays a role in normal neural function. Potentially, this gene product is involved in synapse formation, neurotransmission, learning, cognition, homeostasis, or neuronal differentiation or survival. Moreover, the gene or gene product may also play a role in the treatment and/or detection of developmental disorders associated with the developing embryo, sexually-linked disorders, or disorders of the cardiovascular system. Protein, as well as, antibodies directed against the protein may show utility as a tumor marker and/or immunotherapy targets for the above listed tissues.

Many polynucleotide sequences, such as EST sequences, are publicly available and accessible through sequence databases. Some of these sequences are related to SEQ ID NO:160 and may have been publicly available prior to conception of the present invention. Preferably, such related polynucleotides are specifically excluded from the scope of the present invention. To list every related sequence is cumbersome. Accordingly, preferably excluded from the present invention are one or more polynucleotides comprising a nucleotide sequence described by the general formula of a-b, where a is any integer between 1 to 1828 of SEQ ID NO:160, b is an integer of 15 to 1842, where both a and b correspond to the positions of nucleotide residues shown in SEQ ID NO:160, and where b is greater than or equal to a + 14.

FEATURES OF PROTEIN ENCODED BY GENE NO: 151

The translation product of this gene has been found to have homology to a human DNA mismatch repair protein PMS3 (See Genbank Accession No. R95250).

In specific embodiments, polypeptides of the invention comprise, or alternatively consists of, an amino acid sequence selected from the group: FCHDCKFPEASPAMNCEP (SEQ ID NO:1052), FCHDCKFPEASPAMNCEP (SEQ ID NO:1053), and/or HEPYAVLVI (SEQ ID NO:1054). Moreover, fragments and variants of these polypeptides (such as, for example, fragments as described herein, polypeptides at least 80%, 85%, 90%, 95%, 96%, 97%, 98%, or 99% identical to these polypeptides and polypeptides encoded by the polynucleotide which hybridizes, under stringent conditions, to the polynucleotide encoding these polypeptides) are encompassed by the invention. Antibodies that bind polypeptides of the invention are also encompassed by the invention. Polynucleotides encoding these polypeptides are also encompassed by the invention.

This gene is expressed primarily in neutrophils.

Polynucleotides and polypeptides of the invention are useful as reagents for differential identification of the tissue(s) or cell type(s) present in a biological sample and for diagnosis of diseases and conditions which include, but are not limited to, immune or hematopoietic disorders, such as lymphoma, immunodeficiency diseases, and cancers resulting from genetic instability. Similarly, polypeptides and antibodies directed to these polypeptides are useful in providing immunological probes for differential identification of the tissue(s) or cell type(s). For a number of disorders of the above tissues or cells, particularly of the immune system, expression of this gene at significantly higher or lower levels may be routinely detected in certain tissues or cell types (e.g., immune, hematopoietic, and cancerous and wounded tissues) or bodily fluids (e.g., lymph, serum, plasma, urine, synovial fluid and spinal fluid) or another tissue or cell sample taken from an individual having such a disorder, relative to the standard gene expression level, i.e., the expression level in healthy tissue or bodily fluid from an individual not having the disorder.

Predicted epitopes include those comprising a sequence shown in SEQ ID NO: 399 as residues: Met-1 to Lys-6.

The tissue distribution in neutrophils, combined with the sequence homology to a human mismatch DNA repair enzyme indicates that the protein product of this gene is useful for diagnosis of Hodgkin's lymphoma, since the elevated expression and secretion by the tumor mass may be indicative of tumors of this type. Additionally the gene product may be used as a target in the immunotherapy of the cancer. Because the gene is expressed in cells of lymphoid origin, the natural gene product may be involved in immune functions. Therefore it may be also used as an agent for immunological disorders including arthritis, asthma, immune deficiency diseases such as AIDS, and leukemia. Furthermore, its homology to a known DNA repair protein would suggest the gene may be useful in establishing cancer predisposition and prevention or be of use in gene therapy applications. Protein, as well as, antibodies directed against the protein may show utility as a tumor marker and/or immunotherapy targets for the above listed tissues.

Many polynucleotide sequences, such as EST sequences, are publicly available and accessible through sequence databases. Some of these sequences are related to SEQ ID NO:161 and may have been publicly available prior to conception of the present invention. Preferably, such related polynucleotides are specifically excluded from the scope of the present invention. To list every related sequence is cumbersome. Accordingly, preferably excluded from the present invention are one or more polynucleotides comprising a nucleotide sequence described by the general formula of a-b, where a is any integer between 1 to 756 of SEQ ID NO:161, b is an integer of 15 to 770, where both a and b correspond to the positions of nucleotide residues shown in SEQ ID NO:161, and where b is greater than or equal to a + 14.

FEATURES OF PROTEIN ENCODED BY GENE NO: 152

In specific embodiments, polypeptides of the invention comprise, or alternatively consists of, the following amino acid sequence: PQPSNFPTTVRNLPYSGAGAQPPPSNC (SEQ ID NO:1055). Moreover, fragments

and variants of this polypeptide (such as, for example, fragments as described herein, polypeptides at least 80%, 85%, 90%, 95%, 96%, 97%, 98%, or 99% identical to these polypeptides and polypeptides encoded by the polynucleotide which hybridize, under stringent conditions, to the polynucleotide encoding this polypeptide are encompassed by the invention. Antibodies that bind polypeptides of the invention are also encompassed by the invention. Polynucleotides encoding this polypeptide are also encompassed by the invention.

This gene is expressed primarily in neutrophils.

Polynucleotides and polypeptides of the invention are useful as reagents for differential identification of the tissue(s) or cell type(s) present in a biological sample and for diagnosis of diseases and conditions which include, but are not limited to, immune or hematopoietic disorders, such as infectious diseases and lymphoma. Similarly, polypeptides and antibodies directed to these polypeptides are useful in providing immunological probes for differential identification of the tissue(s) or cell type(s). For a number of disorders of the above tissues or cells, particularly of the immune system, expression of this gene at significantly higher or lower levels may be routinely detected in certain tissues or cell types (e.g., immune, hematopoietic, and cancerous and wounded tissues) or bodily fluids (e.g., lymph, serum, plasma, urine, synovial fluid and spinal fluid) or another tissue or cell sample taken from an individual having such a disorder, relative to the standard gene expression level, i.e., the expression level in healthy tissue or bodily fluid from an individual not having the disorder.

The tissue distribution in neutrophils indicates that the protein product of this gene is useful for the treatment of inflammation and infectious diseases. Expression of this gene product in neutrophils indicates a role in regulating the proliferation; survival; differentiation; and/or activation of hematopoietic cell lineages, including blood stem cells. This gene product may be involved in the regulation of cytokine production, antigen presentation, or other processes that may also suggest a usefulness in the treatment of cancer (e.g. by boosting immune responses). Since the gene is expressed in cells of lymphoid origin, the natural gene product may be involved in immune functions. Therefore it may be also used as an agent for immunological disorders including arthritis, asthma, immunodeficiency diseases such

as AIDS, leukemia, rheumatoid arthritis, granulomatous disease, inflammatory bowel disease, sepsis, acne, neutropenia, neutrophilia, psoriasis, hypersensitivities, such as T-cell mediated cytotoxicity; immune reactions to transplanted organs and tissues, such as host-versus-graft and graft-versus-host diseases, or autoimmunity disorders, such as autoimmune infertility, lens tissue injury, demyelination, systemic lupus erythematosis, drug induced hemolytic anemia, rheumatoid arthritis, Sjogren's disease, scleroderma and tissues. In addition, this gene product may have commercial utility in the expansion of stem cells and committed progenitors of various blood lineages, and in the differentiation and/or proliferation of various cell types. Protein, as well as, antibodies directed against the protein may show utility as a tumor marker and/or immunotherapy targets for the above listed tissues.

Many polynucleotide sequences, such as EST sequences, are publicly available and accessible through sequence databases. Some of these sequences are related to SEQ ID NO:162 and may have been publicly available prior to conception of the present invention. Preferably, such related polynucleotides are specifically excluded from the scope of the present invention. To list every related sequence is cumbersome. Accordingly, preferably excluded from the present invention are one or more polynucleotides comprising a nucleotide sequence described by the general formula of a-b, where a is any integer between 1 to 505 of SEQ ID NO:162, b is an integer of 15 to 519, where both a and b correspond to the positions of nucleotide residues shown in SEQ ID NO:162, and where b is greater than or equal to a + 14.

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FEATURES OF PROTEIN ENCODED BY GENE NO: 153

In specific embodiments, polypeptides of the invention comprise, or alternatively consists of, an amino acid sequence selected from the group: MASSVPAGGHTRAGGIFLIGKLDLEASLFKSFQWLPFVLRKKCNFFCWDSSA HSLPLHPLSASCSAPACHASDTHLLYPSTRALCPSIFAWLVAPHSVFRTNAPGP TPSSQSSPVFPVFPVSFMALIVCXLVCC (SEQ ID NO:1056), MASSVPAGGHTRAGGIFLIGKLDLEASLFKSFQWLPFVLRKKCNFFCWDSSA HSLPLHPLSASCSAPACHA (SEQ ID NO:1057),

FAWLVAPHSVFRTNAPGPTPSSQSSPVFPVFPVSFMALIVCXLVCC (SEQ ID NO:1058),
MASSVPAGGHTRAGGIFLIGKLDLEASLFKSFQWLPFVLRKKCNFFCWDSSA HSLPLHPLSASCSAPACHASDTHLLYPSTRALCPSIFAWLVAPHSVFRTNAPGP TPSSQSSPVFPVFPVSFMALIVCXLVCC (SEQ ID NO:1059), LVNWILKLHCLNLFSGFPLYLEKNATSSAGTHPLTAFPSTLSLPHALPLPAMPP ILTFCTPAPVPSAPRSLPGWLLLTQCSGQMLLALPHLASLARSSLSSLFHSWLL LFVXLCAVDF (SEQ ID NO:1060), NLFSGFPLYLEKNATSSAGTHPL (SEQ ID NO:1061), and/or PHLASLARSSLSSLFHSWLLL (SEQ ID NO:1062). Moreover, fragments and variants of these polypeptides (such as, for example, fragments as described herein, polypeptides at least 80%, 85%, 90%, 95%, 96%, 97%, 98%, or 99% identical to these polypeptides and polypeptides encoded by the polynucleotide which hybridizes, under stringent conditions, to the polynucleotide encoding these polypeptides) are encompassed by the invention. Antibodies that bind polypeptides of the invention are also encompassed by the invention. Polynucleotides encoding these polypeptides are also encompassed by the invention.

This gene is expressed primarily in neutrophils.

Polynucleotides and polypeptides of the invention are useful as reagents for differential identification of the tissue(s) or cell type(s) present in a biological sample and for diagnosis of diseases and conditions which include, but are not limited to, immune or hematopoietic disorders, such as inflammation and infectious diseases. Similarly, polypeptides and antibodies directed to these polypeptides are useful in providing immunological probes for differential identification of the tissue(s) or cell type(s). For a number of disorders of the above tissues or cells, particularly of the immune system, expression of this gene at significantly higher or lower levels may be routinely detected in certain tissues or cell types (e.g., immune, hematopoietic, and cancerous and wounded tissues) or bodily fluids (e.g., lymph, serum, plasma, urine, synovial fluid and spinal fluid) or another tissue or cell sample taken from an individual having such a disorder, relative to the standard gene expression level, i.e., the expression level in healthy tissue or bodily fluid from an individual not having the disorder.

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Predicted epitopes include those comprising a sequence shown in SEQ ID NO: 401 as residues: Ser-11 to Pro-17.

The tissue distribution in neutrophils indicates that the protein product of this gene is useful for the treatment of infectious diseases and inflammation. Moreover, the expression of this gene product indicates a role in regulating the proliferation; survival; differentiation; and/or activation of hematopoietic cell lineages, including blood stem cells. This gene product may be involved in the regulation of cytokine production, antigen presentation, or other processes that may also suggest a usefulness in the treatment of cancer (e.g. by boosting immune responses). Since the gene is expressed in cells of lymphoid origin, the natural gene product may be involved in immune functions. Therefore it may be also used as an agent for immunological disorders including arthritis, asthma, immunodeficiency diseases such as AIDS, leukemia, rheumatoid arthritis, granulomatous disease, inflammatory bowel disease, sepsis, acne, neutropenia, neutrophilia, psoriasis, hypersensitivities, such as T-cell mediated cytotoxicity; immune reactions to transplanted organs and tissues, such as host-versus-graft and graft-versus-host diseases, or autoimmunity disorders, such as autoimmune infertility, lens tissue injury, demyelination, systemic lupus erythematosis, drug induced hemolytic anemia, rheumatoid arthritis, Sjogren's disease, scleroderma and tissues. In addition, this gene product may have commercial utility in the expansion of stem cells and committed progenitors of various blood lineages, and in the differentiation and/or proliferation of various cell types. Protein, as well as, antibodies directed against the protein may show utility as a tumor marker and/or immunotherapy targets for the above listed tissues.

Many polynucleotide sequences, such as EST sequences, are publicly available and accessible through sequence databases. Some of these sequences are related to SEQ ID NO:163 and may have been publicly available prior to conception of the present invention. Preferably, such related polynucleotides are specifically excluded from the scope of the present invention. To list every related sequence is cumbersome. Accordingly, preferably excluded from the present invention are one or more polynucleotides comprising a nucleotide sequence described by the general formula of a-b, where a is any integer between 1 to 739 of SEQ ID NO:163, b is an

integer of 15 to 753, where both a and b correspond to the positions of nucleotide residues shown in SEQ ID NO:163, and where b is greater than or equal to a + 14.

FEATURES OF PROTEIN ENCODED BY GENE NO: 154

This gene is primarily expressed in ovary, uterus, adipose tissue, brain, and the liver.

Polynucleotides and polypeptides of the invention are useful as reagents for differential identification of the tissue(s) or cell type(s) present in a biological sample and for diagnosis of diseases and conditions which include, but are not limited to, reproductive, neural, hepatic, and metabolic disorders. Similarly, polypeptides and antibodies directed to these polypeptides are useful in providing immunological probes for differential identification of the tissue(s) or cell type(s). For a number of disorders of the above tissues or cells, particularly of the female reproductive system, expression of this gene at significantly higher or lower levels may be routinely detected in certain tissues or cell types (e.g., ovary, uterus, adipose tissue, brain, liver, and cancerous and wounded tissues) or bodily fluids (e.g., lymph, bile, amniotic fluid, serum, plasma, urine, synovial fluid and spinal fluid) or another tissue or cell sample taken from an individual having such a disorder, relative to the standard gene expression level, i.e., the expression level in healthy tissue or bodily fluid from an individual not having the disorder.

Predicted epitopes include those comprising a sequence shown in SEQ ID NO: 402 as residues: Asn-56 to Gly-67.

The tissue distribution of this gene product in ovary and uterus indicates that the protein product of this gene is useful for diagnostic or therapeutic uses in the treatment of the female reproductive system, obesity, and liver disorders, particularly cancer in the above tissues. Protein, as well as, antibodies directed against the protein may show utility as a tumor marker and/or immunotherapy targets for the above listed tissues.

Many polynucleotide sequences, such as EST sequences, are publicly available and accessible through sequence databases. Some of these sequences are

related to SEQ ID NO:164 and may have been publicly available prior to conception of the present invention. Preferably, such related polynucleotides are specifically excluded from the scope of the present invention. To list every related sequence is cumbersome. Accordingly, preferably excluded from the present invention are one or more polynucleotides comprising a nucleotide sequence described by the general formula of a-b, where a is any integer between 1 to 1879 of SEQ ID NO:164, b is an integer of 15 to 1893, where both a and b correspond to the positions of nucleotide residues shown in SEQ ID NO:164, and where b is greater than or equal to a + 14.

FEATURES OF PROTEIN ENCODED BY GENE NO: 155

The gene encoding the disclosed cDNA is believed to reside on chromosome 3. Accordingly, polynucleotides related to this invention are useful as a marker in linkage analysis for chromosome 3.

This gene is expressed in multiple tissues including brain, aortic endothelial cells, smooth muscle, pituitary, testis, melanocytes, spleen, neutrophils, and placenta.

Polynucleotides and polypeptides of the invention are useful as reagents for differential identification of the tissue(s) or cell type(s) present in a biological sample and for diagnosis of diseases and conditions which include, but are not limited to, immunological or vascular disorders, including immunodeficiencies, cancers of the brain and the female reproductive system, as well as cardiovascular disorders, such as atherosclerosis and stroke. Similarly, polypeptides and antibodies directed to these polypeptides are useful in providing immunological probes for differential identification of the tissue(s) or cell type(s). For a number of disorders of the above tissues or cells, particularly of the central nervous and immune systems, expression of this gene at significantly higher or lower levels may be routinely detected in certain tissues or cell types (e.g., immune, vascular, endothelial, neural, hematopoietic, reproductive, integumentary, placental, endocrine, and cancerous and wounded tissues) or bodily fluids (e.g., lymph, amniotic fluid, serum, plasma, urine, synovial fluid and spinal fluid) or another tissue or cell sample taken from an individual having

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such a disorder, relative to the standard gene expression level, i.e., the expression level in healthy tissue or bodily fluid from an individual not having the disorder.

The tissue distribution in neural tissue indicates that the protein product of this gene is useful in the treatment/detection of disorders in the nervous system, including schizophrenia, neurodegeneration, neoplasia, brain cancer as well as vascular and female reproductive disorders, including cancer within the above tissues. Moreover, the protein product of this gene may also be useful in the treatment and/or detection of other vascular disorders which include, but are not limited to, aneurysms, emboli, thrombosis, atherosclerosis, microvascular disease, or stroke. Protein, as well as, antibodies directed against the protein may show utility as a tumor marker and/or immunotherapy targets for the above listed tissues.

Many polynucleotide sequences, such as EST sequences, are publicly available and accessible through sequence databases. Some of these sequences are related to SEQ ID NO:165 and may have been publicly available prior to conception of the present invention. Preferably, such related polynucleotides are specifically excluded from the scope of the present invention. To list every related sequence is cumbersome. Accordingly, preferably excluded from the present invention are one or more polynucleotides comprising a nucleotide sequence described by the general formula of a-b, where a is any integer between 1 to 2139 of SEQ ID NO:165, b is an integer of 15 to 2153, where both a and b correspond to the positions of nucleotide residues shown in SEQ ID NO:165, and where b is greater than or equal to a + 14.

FEATURES OF PROTEIN ENCODED BY GENE NO: 156

The translation product of this gene shares sequence homology with the human gene encoding cytochrome b561 (See Genbank Accession No. P10897). Cytochrome b561 is a transmembrane electron transport protein that is specific to a subset of secretory vesicles containing catecholamines and amidated peptides. This protein is thought to supply reducing equivalents to the intravesicular enzymes dopamine-beta-hydroxylase and alpha-peptide amidase.

In specific embodiments, polypeptides of the invention comprise, or alternatively consists of, an amino acid sequence selected from the group: MAMEGYWRFLALLGSALLVGFLSVIFALVWVLHYREGLGWDGSALEFNWH PVLMVTGFVFIQGIAIIVYRLPWTWKCSKLLMKSIHAGLNAVAAILAIISVVAV FENHNVNNIANMYSLHSWVGLIAVICYLLQLLSGFSVFLLPWAPLSLRAFLMP IHVYSGIVIFGTVIATALMGLTEKLIFSLRDPAYSTFPPEGVFVNTLGLLILVFG ALIFWIVTRPQWKRPKEPNSTILHPNGGTEQGARGSMPAYSGNNMDKSDSEL NSEVAARKRNLALDEAGQRSTM (SEQ ID NO:1063), AHASAHASGGAEYGAL (SEQ ID NO:1064), QYSQYVQSAQLGWTDSCHMLFVTASFRFFSLSASMGSAFSPSISHAHTCLFW NCHLWNSDCNSTYGIDRETDFFPERSCIQYIPARRCFRKYAWPSDPGVRGPHF LDSHQTAMETS (SEQ ID NO:1065), ASMGS AFSPSISHAHTCLFWNCHLWNSDCNSTYG (SEQ ID NO:1066), FVHVVARVGWHGTSCSLFSASIWMKNGRIWLLRTFPLRSGDYPKNEGPEHQ DQKAKRIYENTFWRECTVCRISQGKNQFLCQSHKCCCNHCSKDDNSRINMY GHEKCSERKRSPWKQKD (SEQ ID NO:1067), and/or ASIWMKNGRIWLLRTFPLRSGDYPKNEGPEHQ (SEQ ID NO:1068). Moreover, fragments and variants of these polypeptides (such as, for example, fragments as described herein, polypeptides at least 80%, 85%, 90%, 95%, 96%, 97%, 98%, or 99% identical to these polypeptides and polypeptides encoded by the polynucleotide which hybridizes, under stringent conditions, to the polynucleotide encoding these polypeptides) are encompassed by the invention. Antibodies that bind polypeptides of the invention are also encompassed by the invention. Polynucleotides encoding these polypeptides are also encompassed by the invention.

The gene encoding the disclosed cDNA is believed to reside on chromosome 2. Accordingly, polynucleotides related to this invention are useful as a marker in linkage analysis for chromosome 2.

This gene is expressed primarily in anergic T-cells.

Polynucleotides and polypeptides of the invention are useful as reagents for differential identification of the tissue(s) or cell type(s) present in a biological sample and for diagnosis of diseases and conditions which include, but are not limited to, immune or hematopoietic disorders, and metabolic related diseases. Similarly,

polypeptides and antibodies directed to these polypeptides are useful in providing immunological probes for differential identification of the tissue(s) or cell type(s). For a number of disorders of the above tissues or cells, particularly of the immune system, expression of this gene at significantly higher or lower levels may be routinely detected in certain tissues or cell types (e.g., immune, hematopoietic, metabolic, and cancerous and wounded tissues) or bodily fluids (e.g., lymph, serum, plasma, urine, synovial fluid and spinal fluid) or another tissue or cell sample taken from an individual having such a disorder, relative to the standard gene expression level, i.e., the expression level in healthy tissue or bodily fluid from an individual not having the disorder.

Predicted epitopes include those comprising a sequence shown in SEQ ID NO: 404 as residues: Pro-222 to Asn-231, Asn-238 to Gly-247, Ala-251 to Leu-264, Ala-280 to Thr-285.

The tissue distribution in anergic T-cells indicates that the protein product or mRNA of this gene is useful for the treatment or diagnosis of immune system and metabolic diseases or conditions including Tay-Sachs disease, phenylketonuria, galactosemia, various porphyrias, and Hurler's syndrome. Protein, as well as, antibodies directed against the protein may show utility as a tumor marker and/or immunotherapy targets for the above listed tissues.

Many polynucleotide sequences, such as EST sequences, are publicly available and accessible through sequence databases. Some of these sequences are related to SEQ ID NO:166 and may have been publicly available prior to conception of the present invention. Preferably, such related polynucleotides are specifically excluded from the scope of the present invention. To list every related sequence is cumbersome. Accordingly, preferably excluded from the present invention are one or more polynucleotides comprising a nucleotide sequence described by the general formula of a-b, where a is any integer between 1 to 1237 of SEQ ID NO:166, b is an integer of 15 to 1251, where both a and b correspond to the positions of nucleotide residues shown in SEQ ID NO:166, and where b is greater than or equal to a + 14.

FEATURES OF PROTEIN ENCODED BY GENE NO: 157

The translation product of this gene shares sequence homology with collagen which is important in mammalian development. This gene also shows sequence homology with bcl-2 and the HNK-1 sulfotransferase of Rattus norvegicus which is thought be involved in carbohydrate biosynthesis. (See Genbank Accession No. P80988 and AF022729, respectively.) When tested against Jurkat cell lines, supernatants removed from cells containing this gene activated the GAS (gamma activating sequence) promoter element. Thus, it is likely that this gene activates T-cells cells through the JAK-STAT signal transduction pathway. GAS is a promoter element found upstream of many genes which are involved in the Jak-STAT pathway. The Jak-STAT pathway is a large, signal transduction pathway involved in the differentiation and proliferation of cells. Therefore, activation of the Jak-STAT pathway, reflected by the binding of the GAS element, can be used to indicate proteins involved in the proliferation and differentiation of cells.

In specific embodiments, polypeptides of the invention comprise, or alternatively consists of, the following amino acid sequence: PGRAGPSPGLSLQLPAEPGHPAGNLAPLTSRPQPLCRIPAVPG (SEQ ID NO:1069). Moreover, fragments and variants of this polypeptide (such as, for example, fragments as described herein, polypeptides at least 80%, 85%, 90%, 95%, 96%, 97%, 98%, or 99% identical to these polypeptides and polypeptides encoded by the polynucleotide which hybridize, under stringent conditions, to the polynucleotide encoding this polypeptide are encompassed by the invention. Antibodies that bind polypeptides of the invention are also encompassed by the invention. Polynucleotides encoding this polypeptide are also encompassed by the invention.

This gene is expressed primarily in HL-60 tissue culture cells, and to a lesser extent, in liver, breast, and uterus.

Polynucleotides and polypeptides of the invention are useful as reagents for differential identification of the tissue(s) or cell type(s) present in a biological sample and for diagnosis of diseases and conditions which include, but are not limited to, immunological diseases, hereditary disorders involving the MHC class of immune molecules, as well as developmental disorders and reproductive disorders. Similarly, polypeptides and antibodies directed to these polypeptides are useful in providing

immunological probes for differential identification of the tissue(s) or cell type(s). For a number of disorders of the above tissues or cells, particularly of the immune and reproductive system expression of this gene at significantly higher or lower levels may be routinely detected in certain tissues or cell types (e.g., reproductive, hepatic, immune, hematopoietic, and cancerous and wounded tissues) or bodily fluids (e.g., lymph, serum, plasma, urine, synovial fluid and spinal fluid) or another tissue or cell sample taken from an individual having such a disorder, relative to the standard gene expression level, i.e., the expression level in healthy tissue or bodily fluid from an individual not having the disorder.

Predicted epitopes include those comprising a sequence shown in SEQ ID NO: 405 as residues: Ser-39 to Gly-46, Leu-49 to Ala-62.

The tissue distribution in reproductive, and immune tissues, combined with the homology to collagen and the detected GAS biological activity indicates that the protein product of this gene is useful for diagnosis and treatment of hereditary MHC disorders and particularly autoimmune disorders including rheumatoid arthritis, lupus, scleroderma, and dermatomyositis, as well as many reproductive disorders, including cancer of the uterus, and breast tissues. Protein, as well as, antibodies directed against the protein may show utility as a tumor marker and/or immunotherapy targets for the above listed tissues.

Many polynucleotide sequences, such as EST sequences, are publicly available and accessible through sequence databases. Some of these sequences are related to SEQ ID NO:167 and may have been publicly available prior to conception of the present invention. Preferably, such related polynucleotides are specifically excluded from the scope of the present invention. To list every related sequence is cumbersome. Accordingly, preferably excluded from the present invention are one or more polynucleotides comprising a nucleotide sequence described by the general formula of a-b, where a is any integer between 1 to 868 of SEQ ID NO:167, b is an integer of 15 to 882, where both a and b correspond to the positions of nucleotide residues shown in SEQ ID NO:167, and where b is greater than or equal to a + 14.

FEATURES OF PROTEIN ENCODED BY GENE NO: 158

This gene is expressed primarily in the amygdala region of the brain.

Polynucleotides and polypeptides of the invention are useful as reagents for differential identification of the tissue(s) or cell type(s) present in a biological sample and for diagnosis of diseases and conditions which include, but are not limited to, a variety of brain disorders, particularly those effecting mood and personality, in addition to neurodegenerative conditions. Similarly, polypeptides and antibodies directed to these polypeptides are useful in providing immunological probes for differential identification of the tissue(s) or cell type(s). For a number of disorders of the above tissues or cells, particularly of the brain and central nervous system, expression of this gene at significantly higher or lower levels may be routinely detected in certain tissues or cell types (e.g., neural, and cancerous and wounded tissues) or bodily fluids (e.g., lymph, serum, plasma, urine, synovial fluid and spinal fluid) or another tissue or cell sample taken from an individual having such a disorder, relative to the standard gene expression level, i.e., the expression level in healthy tissue or bodily fluid from an individual not having the disorder.

The tissue distribution in the amygdala indicates that the protein product of this gene is useful for the treatment and/or diagnosis of a variety of brain disorders, particularly bi-polar disorder, uni-polar depression, and dementia. Moreover, The tissue distribution indicates that the protein product of this gene is useful for the detection/treatment of neurodegenerative disease states, behavioral disorders, or inflammatory conditions which include, but are not limited to Alzheimer's Disease, Parkinson's Disease, Huntington's Disease, Tourette's Syndrome, meningitis, encephalitis, demyelinating diseases, peripheral neuropathies, neoplasia, trauma, congenital malformations, spinal cord injuries, ischemia and infarction, aneurysms, hemorrhages, schizophrenia, mania, dementia, paranoia, obsessive compulsive disorder, panic disorder, learning disabilities, ALS, psychoses, autism, and altered behaviors, including disorders in feeding, sleep patterns, balance, and perception. In addition, elevated expression of this gene product in regions of the brain indicates that it plays a role in normal neural function. Potentially, this gene product is involved in synapse formation, neurotransmission, learning, cognition, homeostasis, or neuronal differentiation or survival. Moreover, the gene or gene product may also play a role

in the treatment and/or detection of developmental disorders associated with the developing embryo, sexually-linked disorders, or disorders of the cardiovascular system. Protein, as well as, antibodies directed against the protein may show utility as a tumor marker and/or immunotherapy targets for the above listed tissues.

Many polynucleotide sequences, such as EST sequences, are publicly available and accessible through sequence databases. Some of these sequences are related to SEQ ID NO:168 and may have been publicly available prior to conception of the present invention. Preferably, such related polynucleotides are specifically excluded from the scope of the present invention. To list every related sequence is cumbersome. Accordingly, preferably excluded from the present invention are one or more polynucleotides comprising a nucleotide sequence described by the general formula of a-b, where a is any integer between 1 to 1194 of SEQ ID NO:168, b is an integer of 15 to 1208, where both a and b correspond to the positions of nucleotide residues shown in SEQ ID NO:168, and where b is greater than or equal to a + 14.

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FEATURES OF PROTEIN ENCODED BY GENE NO: 159

This gene is expressed in a variety of tissues and cell types including brain, smooth muscle, kidney, salivary gland, and T-cells.

Polynucleotides and polypeptides of the invention are useful as reagents for differential identification of the tissue(s) or cell type(s) present in a biological sample and for diagnosis of diseases and conditions which include, but are not limited to, neural, renal, vascular, metabolic, or immune disorders, particularly cancers. Similarly, polypeptides and antibodies directed to these polypeptides are useful in providing immunological probes for differential identification of the tissue(s) or cell type(s). For a number of disorders of the above tissues or cells, particularly of the central nervous, urinary, salivary, digestive, and immune systems, expression of this gene at significantly higher or lower levels may be routinely detected in certain tissues or cell types (e.g., neural, renal, vascular, metabolic, immune cancerous and wounded tissues) or bodily fluids (e.g., lymph, serum, plasma, urine, synovial fluid and spinal fluid) or another tissue or cell sample taken from an individual having such

a disorder, relative to the standard gene expression level, i.e., the expression level in healthy tissue or bodily fluid from an individual not having the disorder.

Predicted epitopes include those comprising a sequence shown in SEQ ID NO: 407 as residues: Asp-43 to Asp-60.

The tissue distribution in brain, smooth muscle, and T-cells indicates that the protein product of this gene is useful for diagnosis of various neurological, and cardiovascular disorders, but not limited to cancer within the above tissues. Additionally the gene product may be used as a target in the immunotherapy of the cancer. Because the gene is expressed in cells of lymphoid origin, the natural gene product may be involved in immune functions. Therefore it may be also used as an agent for immunological disorders including arthritis, asthma, immune deficiency diseases such as AIDS, and leukemia. Protein, as well as, antibodies directed against the protein may show utility as a tumor marker and/or immunotherapy targets for the above listed tissues.

Many polynucleotide sequences, such as EST sequences, are publicly available and accessible through sequence databases. Some of these sequences are related to SEQ ID NO:169 and may have been publicly available prior to conception of the present invention. Preferably, such related polynucleotides are specifically excluded from the scope of the present invention. To list every related sequence is cumbersome. Accordingly, preferably excluded from the present invention are one or more polynucleotides comprising a nucleotide sequence described by the general formula of a-b, where a is any integer between 1 to 1244 of SEQ ID NO:169, b is an integer of 15 to 1258, where both a and b correspond to the positions of nucleotide residues shown in SEQ ID NO:169, and where b is greater than or equal to a + 14.

FEATURES OF PROTEIN ENCODED BY GENE NO: 160

The translation product of this gene shares sequence homology with collagen, which is thought to be important in cellular interactions, extracellular matrix formation, and has been found to be an identifying determinant in autoimmune disorders. Moreover, this gene shows sequence homology with the yeast protein,

Sls1p, an endoplasmic reticulum component involved in the protein translocation process in the Yeast Yarrowia lipolytica. (See Genbank Accession No. 1052828; see also J. Biol. Chem. 271, 11668-11675 (1996).) In Mus musculus, this same region shows sequence homology with the heavy chain of kinesin. (See Genbank Accession No. 2062607.) Recently, suppression of the heavy chain of kinesin was shown to inhibit insulin secretion from primary cultures of mouse beta-cells. (See Endocrinology 138 (5), 1979-1987 (1997).) Moreover, kinesin was found associated with drug resistance and cell immortalization. (See Genbank Accession No. 468355.) Thus, it is likely that this gene also acts as a genetic suppressor element.

In specific embodiments, polypeptides of the invention comprise, or alternatively consists of, an amino acid sequence selected from the group: ARGRRRGRLELWELCLPLGCRRRRSLTMAPQSLPSSRMAPLG (SEQ ID NO:1070),

NGQASTAKMSSCLRSPPTLAPLSLTSGIPVQSWCGASSQLLQQAVDRAQQLL EVALVLTILQLQAGQHLVLSLQAGQCPAELGVLTVAVPAGGQEDAQCLQHL LTGIMLGQRQEVGRDLAPALFPQAWQEVYLAILLQLLWGHLLGQLSLLLGEH LLRDQVVEQCDHAHGEHLRALLLHQGPQDLQPPELQELPLGIGEVAQQGAQ CKQDLLLCSERLLRGQDDQQLLQGSPFDGLHLDLGVAGKGSAQHKRSILLHE GLCAVQPIDHHLKTTKGKQVLRIVHLMDIIFKIKERSNLLFQTGAGTIELVDQP YHDLHVSLNDNIQLIKVFLQFLNGAEEPLYLSLPCLVFL (SEQ ID NO:1071), QHLVLSLQAGQCPAELGVLTVAVPAGGQEDAQC (SEQ ID NO:1072), QLSLLLGEHLLRDQVVEQCDHAHGEH (SEQ ID NO:1073), GS PFDGLHLDLGVAGKGSAQHKRSILLHEGLC (SEQ ID NO:1074), and/or HLMDII FKIKERSNLLFQTGAGTIELVDQP (SEQ ID NO:1075). Moreover, fragments and variants of these polypeptides (such as, for example, fragments as described herein, polypeptides at least 80%, 85%, 90%, 95%, 96%, 97%, 98%, or 99% identical to these polypeptides and polypeptides encoded by the polynucleotide which hybridizes, under stringent conditions, to the polynucleotide encoding these polypeptides) are encompassed by the invention. Antibodies that bind polypeptides of the invention are also encompassed by the invention. Polynucleotides encoding these polypeptides are also encompassed by the invention.

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The gene encoding the disclosed cDNA is believed to reside on chromosome 5. Accordingly, polynucleotides related to this invention are useful as a marker in linkage analysis for chromosome 5.

This gene is expressed primarily in the greater omentum, and to a lesser extent in gall bladder, stromal bone marrow cells, lymph node, liver, testes, pituitary, and thymus.

Polynucleotides and polypeptides of the invention are useful as reagents for differential identification of the tissue(s) or cell type(s) present in a biological sample and for diagnosis of diseases and conditions which include, but are not limited to, disorders of the endocrine, gastrointestinal, and immunological systems, including autoimmune disorders and cancers. Similarly, polypeptides and antibodies directed to these polypeptides are useful in providing immunological probes for differential identification of the tissue(s) or cell type(s). For a number of disorders of the above tissues or cells, particularly of the immune and gastrointestinal systems, expression of this gene at significantly higher or lower levels may be routinely detected in certain tissues or cell types (e.g., gastrointestinal, metabolic, immune, hematopoietic, hepatic, reproductive, endocrine, and cancerous and wounded tissues) or bodily fluids (e.g., lymph, bile, serum, plasma, urine, synovial fluid and spinal fluid) or another tissue or cell sample taken from an individual having such a disorder, relative to the standard gene expression level, i.e., the expression level in healthy tissue or bodily fluid from an individual not having the disorder.

Predicted epitopes include those comprising a sequence shown in SEQ ID NO: 408 as residues: Asn-27 to Leu-47, Gln-81 to Lys-88, Asp-93 to Lys-102, Asn-107 to Leu-116, Met-129 to Glu-141, Glu-150 to Asp-157, Lys-176 to Glu-185, Glu-333 to Tyr-349, Cys-393 to Leu-403, Gln-423 to Gly-429.

The tissue distribution within gastrointestinal, endocrine and immunological tissues, combined with the sequence homology to a conserved collagen motif, indicates that the protein product of this gene is useful for the diagnosis of various autoimmune disorders including, but not limited to, rheumatoid arthritis, lupus erythromatosus, scleroderma, and dermatomyositis. Because the gene is expressed in cells of lymphoid origin, the natural gene product may be involved in immune functions. Therefore it may be also used as an agent for immunological disorders

including arthritis, asthma, immune deficiency diseases such as AIDS, and leukemia. Protein, as well as, antibodies directed against the protein may show utility as a tumor marker and/or immunotherapy targets for the above listed tissues.

Many polynucleotide sequences, such as EST sequences, are publicly available and accessible through sequence databases. Some of these sequences are related to SEQ ID NO:170 and may have been publicly available prior to conception of the present invention. Preferably, such related polynucleotides are specifically excluded from the scope of the present invention. To list every related sequence is cumbersome. Accordingly, preferably excluded from the present invention are one or more polynucleotides comprising a nucleotide sequence described by the general formula of a-b, where a is any integer between 1 to 1610 of SEQ ID NO:170, b is an integer of 15 to 1624, where both a and b correspond to the positions of nucleotide residues shown in SEQ ID NO:170, and where b is greater than or equal to a + 14.

09609704 - 050902

FEATURES OF PROTEIN ENCODED BY GENE NO: 161

This gene has homology to the tissue inhibitor of metalloproteinase 2. Such inhibitors are vital to the proper regulation of metalloproteins such as collagenases, which has implications for tissue regeneration and autoimmune disorders (See Genbank Accession No. P16368). When tested against Jurkat cell lines, supernatants removed from cells containing this gene activated the GAS (gamma activating sequence) promoter element. Thus, it is likely that this gene activates T-cells cells through the JAK-STAT signal transduction pathway. GAS is a promoter element found upstream of many genes which are involved in the Jak-STAT pathway. The Jak-STAT pathway is a large, signal transduction pathway involved in the differentiation and proliferation of cells. Therefore, activation of the Jak-STAT pathway, reflected by the binding of the GAS element, can be used to indicate proteins involved in the proliferation and differentiation of cells. In addition, this gene maps to chromosome 17, and therefore, may be used as a marker in linkage analysis for chromosome 17 (See Genbank Accession No. P16368).

This gene is expressed primarily in several types of cancers including osteoclastoma, chondrosarcoma, and rhabdomyosarcoma, and to a lesser extent, in non-malignant tissues including synovium, amygdala, testes, and placenta.

Polynucleotides and polypeptides of the invention are useful as reagents for differential identification of the tissue(s) or cell type(s) present in a biological sample and for diagnosis of diseases and conditions which include, but are not limited to, immune or integumentary disorders, particularly cancers of bone and cartilage, as well as various autoimmune disorders. Similarly, polypeptides and antibodies directed to these polypeptides are useful in providing immunological probes for differential identification of the tissue(s) or cell type(s). For a number of disorders of the above tissues or cells, particularly of the musculoskeletal system, expression of this gene at significantly higher or lower levels may be routinely detected in certain tissues or cell types (e.g., skeletal, integumentary, synovium, muscle, fibroids, reproductive, neural, and cancerous and wounded tissues) or bodily fluids (e.g., lymph, serum, plasma, urine, synovial fluid and spinal fluid) or another tissue or cell sample taken from an individual having such a disorder, relative to the standard gene expression level, i.e., the expression level in healthy tissue or bodily fluid from an individual not having the disorder.

Predicted epitopes include those comprising a sequence shown in SEQ ID NO: 409 as residues: Thr-24 to Thr-34.

The tissue distribution in various cancers, combined with the sequence homology to a collagenase inhibitor and the detected GAS biological activity, indicates that the protein product of this gene is useful for the detection of various autoimmune disorders such as rheumatoid arthritis, lupus, scleroderma, and dermatomyositis. Therefore it may be also used as an agent for immunological disorders including arthritis, asthma, immune deficiency diseases such as AIDS, and leukemia. The expression of this gene product would also suggest a role in the detection and treatment of disorders and conditions afflicting the skeletal system, in particular osteoporosis, bone cancer, as well as, connective tissue disorders (e.g. arthritis, trauma, tendonitis, chrondomalacia and inflammation), such as in the diagnosis or treatment of various autoimmune disorders such as rheumatoid arthritis, lupus, scleroderma, and dermatomyositis as well as dwarfism, spinal deformation, and

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specific joint abnormalities as well as chondrodysplasias (i.e. spondyloepiphyseal dysplasia congenita, familial osteoarthritis, Atelosteogenesis type II, metaphyseal chondrodysplasia type Schmid). Protein, as well as, antibodies directed against the protein may show utility as a tumor marker and/or immunotherapy targets for the above listed tissues.

Many polynucleotide sequences, such as EST sequences, are publicly available and accessible through sequence databases. Some of these sequences are related to SEQ ID NO:171 and may have been publicly available prior to conception of the present invention. Preferably, such related polynucleotides are specifically excluded from the scope of the present invention. To list every related sequence is cumbersome. Accordingly, preferably excluded from the present invention are one or more polynucleotides comprising a nucleotide sequence described by the general formula of a-b, where a is any integer between 1 to 1989 of SEQ ID NO:171, b is an integer of 15 to 2003, where both a and b correspond to the positions of nucleotide residues shown in SEQ ID NO:171, and where b is greater than or equal to a + 14.

09509490.1 - 080200

FEATURES OF PROTEIN ENCODED BY GENE NO: 162

This gene is homologous to the mitochondrial ATP6 gene, and therefore is likely a homolog of this gene family (See Genbank Accession No. X76197).

This gene is expressed primarily in brain tissue.

Polynucleotides and polypeptides of the invention are useful as reagents for differential identification of the tissue(s) or cell type(s) present in a biological sample and for diagnosis of diseases and conditions which include, but are not limited to, neural disorders, including, but not limited to, neurodegenerative conditions, Down's syndrome, depression, Schizophrenia, and epilepsy. Similarly, polypeptides and antibodies directed to these polypeptides are useful in providing immunological probes for differential identification of the tissue(s) or cell type(s). For a number of disorders of the above tissues or cells, particularly of the central nervous system, expression of this gene at significantly higher or lower levels may be routinely detected in certain tissues or cell types (e.g., neural, and cancerous and wounded

tissues) or bodily fluids (e.g., lymph, serum, plasma, urine, synovial fluid and spinal fluid) or another tissue or cell sample taken from an individual having such a disorder, relative to the standard gene expression level, i.e., the expression level in healthy tissue or bodily fluid from an individual not having the disorder.

The tissue distribution in brain tissue indicates this gene is useful for diagnosis of various neurological disorders including, but not limited to, brain cancer. Additionally the gene product may be used as a target in the immunotherapy of cancer in the brain as well as for the diagnosis of metabolic disorders such as obesity, Tay-Sachs disease, phenylketonuria and Hurler's Syndrome. Similarly, the protein product of this gene is useful for the detection/treatment of neurodegenerative disease states, behavioral disorders, or inflammatory conditions which include, but are not limited to Alzheimer's Disease, Parkinson's Disease, Huntington's Disease, Tourette's Syndrome, meningitis, encephalitis, demyelinating diseases, peripheral neuropathies, neoplasia, trauma, congenital malformations, spinal cord injuries, ischemia and infarction, aneurysms, hemorrhages, schizophrenia, mania, dementia, paranoia, obsessive compulsive disorder, depression, panic disorder, learning disabilities, ALS, psychoses, autism, and altered behaviors, including disorders in feeding, sleep patterns, balance, and perception. In addition, elevated expression of this gene product in regions of the brain indicates that it plays a role in normal neural function. Potentially, this gene product is involved in synapse formation, neurotransmission, learning, cognition, homeostasis, or neuronal differentiation or survival. Moreover, the gene or gene product may also play a role in the treatment and/or detection of developmental disorders associated with the developing embryo, sexually-linked disorders, or disorders of the cardiovascular system. Protein, as well as, antibodies directed against the protein may show utility as a tumor marker and/or immunotherapy targets for the above listed tissues.

Many polynucleotide sequences, such as EST sequences, are publicly available and accessible through sequence databases. Some of these sequences are related to SEQ ID NO:172 and may have been publicly available prior to conception of the present invention. Preferably, such related polynucleotides are specifically excluded from the scope of the present invention. To list every related sequence is cumbersome. Accordingly, preferably excluded from the present invention are one or

more polynucleotides comprising a nucleotide sequence described by the general formula of a-b, where a is any integer between 1 to 772 of SEQ ID NO:172, b is an integer of 15 to 786, where both a and b correspond to the positions of nucleotide residues shown in SEQ ID NO:172, and where b is greater than or equal to a + 14.

FEATURES OF PROTEIN ENCODED BY GENE NO: 163

The translation product of this gene was found to have homology to the MRS3 and 4 protein of Saccharomyces cerevisiae (See Genbank Accession No. gi|3996), which is known to suppress a splice defect in mitochondrial by possibly serving to modulate the cation-solute concentration in mitochondria.

In specific embodiments, polypeptides of the invention comprise, or alternatively consist of, the following amino acid sequences: DEPCPPPAASCAPPSWRMELRTGSVGSQAVARRMDGDSRDGGGGKDATGSE DYENLPTSASVSTHMTAGAMAGILEHSVMYPVDSVKTRMQSLSPDPKAQYT SIYGALKKIMRTEASGGPCEASTS (SEQ ID NO:1076), RMELRTGSVGSQAVARRMDGDSRDGGGGKDATGS (SEQ ID NO:1077), and/or PVDSVKTRMQSLSPDPKAQYTSIYGAL (SEQ ID NO:1078). Moreover, fragments and variants of these polypeptides (such as, for example, fragments as described herein, polypeptides at least 80%, 85%, 90%, 95%, 96%, 97%, 98%, or 99% identical to these polypeptides and polypeptides encoded by the polynucleotide which hybridizes, under stringent conditions, to the polynucleotide encoding these polypeptides) are encompassed by the invention. Antibodies that bind polypeptides of the invention are also encompassed by the invention. Polynucleotides encoding these polypeptides are also encompassed by the invention.

The gene encoding the disclosed cDNA is believed to reside on chromosome 8. Accordingly, polynucleotides related to this invention are useful as a marker in linkage analysis for chromosome 8.

This gene is expressed primarily in placenta, neutrophils, and microvascular endothelial cells, and to a lesser extent, brain, prostate, spleen, thymus, and bone.

Polynucleotides and polypeptides of the invention are useful as reagents for differential identification of the tissue(s) or cell type(s) present in a biological sample and for diagnosis of diseases and conditions which include, but are not limited to, immune, vascular, or reproductive disorders. Similarly, polypeptides and antibodies directed to these polypeptides are useful in providing immunological probes for differential identification of the tissue(s) or cell type(s). For a number of disorders of the above tissues or cells, particularly of the immune system, expression of this gene at significantly higher or lower levels may be routinely detected in certain tissues or cell types (e.g., immune, hematopoietic, vascular, endothelial, reproductive, neural, skeletal, and cancerous and wounded tissues) or bodily fluids (e.g., lymph, amniotic fluid, serum, plasma, urine, synovial fluid and spinal fluid) or another tissue or cell sample taken from an individual having such a disorder, relative to the standard gene expression level, i.e., the expression level in healthy tissue or bodily fluid from an individual not having the disorder.

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FEATURES OF PROTEIN ENCODED BY GENE NO: 164

The gene encoding the disclosed cDNA is believed to reside on chromosome 7. Accordingly, polynucleotides related to this invention are useful as a marker in linkage analysis for chromosome 7.

This gene is expressed primarily in neutrophils, monocytes, bone marrow, and fetal liver.

Polynucleotides and polypeptides of the invention are useful as reagents for differential identification of the tissue(s) or cell type(s) present in a biological sample and for diagnosis of diseases and conditions which include, but are not limited to, immune system or hematopoietic disorders including, but not limited to, autoimmune disorders such as lupus, leukemia and immunodeficiency disorders . Similarly, polypeptides and antibodies directed to these polypeptides are useful in providing immunological probes for differential identification of the tissue(s) or cell type(s). For a number of disorders of the above tissues or cells, particularly of the immune system, expression of this gene at significantly higher or lower levels may be

routinely detected in certain tissues or cell types (e.g., immune, hematopoietic, hepatic, developmental, and cancerous and wounded tissues) or bodily fluids (e.g., lymph, serum, amniotic fluid, plasma, urine, synovial fluid and spinal fluid) or another tissue or cell sample taken from an individual having such a disorder, relative to the standard gene expression level, i.e., the expression level in healthy tissue or bodily fluid from an individual not having the disorder.

The tissue distribution in various immune system tissues indicates that the protein product of this gene is useful for the diagnosis of various immunological disorders such as Hodgkin's lymphoma, arthritis, asthma, immune deficiency diseases such as AIDS, and leukemia. Moreover, the protein product of this gene is useful for the treatment and diagnosis of hematopoetic related disorders such as anemia, pancytopenia, leukopenia, thrombocytopenia or leukemia since stromal cells are important in the production of cells of hematopoietic lineages. The uses include bone marrow cell ex vivo culture, bone marrow transplantation, bone marrow reconstitution, radiotherapy or chemotherapy of neoplasia. The gene product may also be involved in lymphopoiesis, therefore, it can be used in immune disorders such as infection, inflammation, allergy, immunodeficiency etc. In addition, this gene product may have commercial utility in the expansion of stem cells and committed progenitors of various blood lineages, and in the differentiation and/or proliferation of various cell types. Protein, as well as, antibodies directed against the protein may show utility as a tumor marker and/or immunotherapy targets for the above listed tissues.

Many polynucleotide sequences, such as EST sequences, are publicly available and accessible through sequence databases. Some of these sequences are related to SEQ ID NO:174 and may have been publicly available prior to conception of the present invention. Preferably, such related polynucleotides are specifically excluded from the scope of the present invention. To list every related sequence is cumbersome. Accordingly, preferably excluded from the present invention are one or more polynucleotides comprising a nucleotide sequence described by the general formula of a-b, where a is any integer between 1 to 1355 of SEQ ID NO:174, b is an integer of 15 to 1369, where both a and b correspond to the positions of nucleotide residues shown in SEQ ID NO:174, and where b is greater than or equal to a + 14.

FEATURES OF PROTEIN ENCODED BY GENE NO: 165

The translation product of this gene shares sequence homology with dystrophin which is thought to be defective in both Duchene and Becker Muscular Dystrophy.

In specific embodiments, polypeptides of the invention comprise, or alternatively consists of, an amino acid sequence selected from the group: MKLLGECSSSIDSVKRLEHKLKEEEESLPGFVNLHSTETQTAGVIDRWELLQA QALSKELRMKQNLQKWQQFNSDLNSIWAWLGDTEEELEQLQRLELSTDIQTI ELQIKKLKELQKAVDHRKAIILSINLCSPEFTQADSKESRDLQDRLXQMNGRW DRVCSLLEEWRGLLQDALMQCQGFHEMSHGLLLMLENIDRRKNEIVPIDSNL DAEILQDHHKQLMQIKHELLESQLRVASLQDMSCQLLVNAEGTDCLEAKEK VHVIGNRLKLLLKEVSRHIKELEKLLDVSSSQQDLSSWSSADELDTSGSVSPX SGRSTPNRQKTPRGKCSLSQPGPSVSSPHSRSTKGGSDSSLSEPXPGRSGRGFL FRVLRAALPLQLLLLLLIGLACLVPMSEEDYSCALSNNFARSFHPMLRYTNGP PPL (SEQ ID NO:1079), MKLLGECSSSIDSVKRLEHKLKEEEESLPGFVNLHSTETQTAGVIDRWELLQA QALSKELRMKQNLQKWQQFNSDLNSIWAWLGDTEEELEQLQRLELSTDIQTI ELQIK (SEQ ID NO:1080), KLKELQKAVDHRKAIILSINLCSPEFTQADSKESRDLQDRLXQMNGRWDRVC SLLEEWRGLLQDALMQCQGFHEMSHGLLLMLENIDRRKNEIVPIDSNLDAEIL QDHHKQLMQIKHELLESQLRVASLQDMSCQL (SEQ ID NO:1081), QDMSCQLLVNAEGTDCLEAKEKVHVIGNRLKLLLKEVSRHIKELEKLLDVSS SQQDLSSWSSADELDTSGSVSPXSGRSTPNRQKTPRGKCSLSQPGPSVSSPHS (SEQ ID NO:1082), DSSLSEPXPGRSGRGFLFRVLRAALPLQLLLLLLIGLACLVPMSEEDYSCALSN NFARSFHPMLRYTNGPPPL (SEQ ID NO:1083), QRFLPPGSCXLIRGPQCPRVTDPTTGQSLDDSRFQIQQTENIIRSKTPTGPELDT SYKGY (SEQ ID NO:1084), SISASRLESIGTISFFLLSMFSSIRSKPWLISWKPWHCIRASCSRPRHSSSREHTR

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SQRPFICXKRSCRSRLSLLSAWVNSGLQRLMERMMALRWSTAFWSSLSFLIW SSMVWMSVLSSRRWSCSNSSSVSPSQAQMLFKSELNCCHFWRFCFILNSLLN AWAWRSSHRSITPAVWVSVLCRLTKPGRLSSSSFSLCSSLFTESILLLHSPSSF M (SEQ ID NO:1085), TAFWSSLSFLIWSSMVWMSVLSSRRWSCSNSSSVS (SEQ ID NO:1086), LLNAWAWRSSHRSITPAVWVSVLCRL (SEQ ID NO:1087), LARHVLQRGYSELGFQQLMLYLHKLFVMVLKYLCIKVRINRDNFIFPSVNVL QHKKQTMAHFMETLALHQGILQQAPPLLQQRAHSVPAPIHLXQAILQVPALL AVSLGELRAAEIDGEDDGFAVVHSFLELLELFDLELDGLDVSAEFQTLELFQL LLRVPQPGPDAVQV (SEQ ID NO:1088), YSELGFQQLMLYLHKLFVMVLKYLCIKV (SEQ ID NO:1089), AMVCFLCWRTLTEGK (SEQ ID NO:1091), and/or VHSFLELLELFDLELDGLDVSAEFQTLEL (SEQ ID NO:1090). Moreover, fragments and variants of these polypeptides (such as, for example, fragments as described herein, polypeptides at least 80%, 85%, 90%, 95%, 96%, 97%, 98%, or 99% identical to these polypeptides and polypeptides encoded by the polynucleotide which hybridizes, under stringent conditions, to the polynucleotide encoding these polypeptides) are encompassed by the invention. Antibodies that bind polypeptides of the invention are also encompassed by the invention. Polynucleotides encoding these polypeptides are also encompassed by the invention.

09604794.020702

This gene maps to chromosome 6, and therefore, may be used as a marker in linkage analysis for chromosome 6 (See Genbank Accession No. N62896).

This gene is expressed in numerous tissues including the heart, kidney, and brain.

Polynucleotides and polypeptides of the invention are useful as reagents for differential identification of the tissue(s) or cell type(s) present in a biological sample and for diagnosis of diseases and conditions which include, but are not limited to, musculoskeletal disorders including Muscular Dystrophy and cardiovascular diseases. Similarly, polypeptides and antibodies directed to these polypeptides are useful in providing immunological probes for differential identification of the tissue(s) or cell type(s). For a number of disorders of the above tissues or cells, particularly of the muscle tissues, expression of this gene at significantly higher or lower levels may be routinely detected in certain tissues or cell types (e.g., muscle, heart, and cancerous

and wounded tissues) or bodily fluids (e.g., lymph, serum, plasma, urine, synovial fluid and spinal fluid) or another tissue or cell sample taken from an individual having such a disorder, relative to the standard gene expression level, i.e., the expression level in healthy tissue or bodily fluid from an individual not having the disorder.

The tissue distribution in heart, combined with the homology to the human dystrophin gene indicates that the protein product of this gene is useful for the diagnosis and treatment of Muscular Dystrophy and other muscle disorders, particularly musculodegenerative conditions. Protein, as well as, antibodies directed against the protein may show utility as a tumor marker and/or immunotherapy targets for the above listed tissues.

Many polynucleotide sequences, such as EST sequences, are publicly available and accessible through sequence databases. Some of these sequences are related to SEQ ID NO:175 and may have been publicly available prior to conception of the present invention. Preferably, such related polynucleotides are specifically excluded from the scope of the present invention. To list every related sequence is cumbersome. Accordingly, preferably excluded from the present invention are one or more polynucleotides comprising a nucleotide sequence described by the general formula of a-b, where a is any integer between 1 to 2365 of SEQ ID NO:175, b is an integer of 15 to 2379, where both a and b correspond to the positions of nucleotide residues shown in SEQ ID NO:175, and where b is greater than or equal to a + 14.

09034570.00200

FEATURES OF PROTEIN ENCODED BY GENE NO: 166

In specific embodiments, polypeptides of the invention comprise, or alternatively consist of, the following amino acid sequences: GAGVGTAMPRVPQSAGGAVTWWGVGLSQPSSVQGGARPGTVPGTPGPLPG LSPAPPPQHPPPLPKLFLLCLSXSLPQDFSLLLCLSLDPCPSSTSDL (SEQ ID NO:1092), GTVPGTPGPLPGLSPAPPPQHPPPLPKLFL (SEQ ID NO:1093), APSRCRRSVVQVPYSAFSSCSWTPTALRRGVLLYAGLSTSSASKAQGWHCLG LEYPSGAIMEVRGRGGDRYAQGPSKCWRGCXLVGSGSVTAILCPGWGKAW DSARHPRTPSRLVSCSTASTPPTPAQAVSPLPLXFPAPGLLSSPLPLLGPLPFLY

L (SEQ ID NO:1094), TALRRGVLLYAGLSTSSASKAQGWHCLGLEYPSGAIM (SEQ ID NO:1095), AILCPGWGKAWDSARHPRTPSRLVSCSTASTPP (SEQ ID NO:1096),

PPVFMASHRPXGMEPGEWRFVLVHIAFXCAWDLVCEHVSVCSQVRGRGRA GVQGEAEEKREVLGQGXREAEEKQLGQGWGVLRRWSRRQAWKGSWGAW HCPRPCPTLDRGWL (SEQ ID NO:1097), and/or HVSVCSQVRGRGRAGVQGEAEEKREVLGQ (SEQ ID NO:1098). Moreover, fragments and variants of these polypeptides (such as, for example, fragments as described herein, polypeptides at least 80%, 85%, 90%, 95%, 96%, 97%, 98%, or 99% identical to these polypeptides and polypeptides encoded by the polynucleotide which hybridizes, under stringent conditions, to the polynucleotide encoding these polypeptides) are encompassed by the invention. Antibodies that bind polypeptides of the invention are also encompassed by the invention. Polynucleotides encoding these polypeptides are also encompassed by the invention.

This gene is expressed primarily in human cerebellum.

Polynucleotides and polypeptides of the invention are useful as reagents for differential identification of the tissue(s) or cell type(s) present in a biological sample and for diagnosis of diseases and conditions which include, but are not limited to, diseases of the central nervous system, including Alzheimer's Disease, Parkinson's Disease, ALS, and mental illnesses. Similarly, polypeptides and antibodies directed to these polypeptides are useful in providing immunological probes for differential identification of the tissue(s) or cell type(s). For a number of disorders of the above tissues or cells, particularly of the central nervous system, expression of this gene at significantly higher or lower levels may be routinely detected in certain tissues or cell types (e.g., neural, and cancerous and wounded tissues) or bodily fluids (e.g., lymph, serum, plasma, urine, synovial fluid and spinal fluid) or another tissue or cell sample taken from an individual having such a disorder, relative to the standard gene expression level, i.e., the expression level in healthy tissue or bodily fluid from an individual not having the disorder.

Predicted epitopes include those comprising a sequence shown in SEQ ID NO: 414 as residues: Pro-20 to Gly-26, Leu-37 to Pro-42, His-57 to Gly-63.

09034504.030502

The tissue distribution in human cerebellum indicates that the protein products of this gene are useful for the treatment/diagnosis of diseases of the central nervous system and may protect or enhance survival of neuronal cells by slowing progression of neurodegenerative diseases. Moreover, the protein product of this gene is useful for the detection/treatment of neurodegenerative disease states, behavioral disorders, or inflammatory conditions which include, but are not limited to Alzheimer's Disease, Parkinson's Disease, Huntington's Disease, Tourette's Syndrome, meningitis, encephalitis, demyelinating diseases, peripheral neuropathies, neoplasia, trauma, congenital malformations, spinal cord injuries, ischemia and infarction, aneurysms, hemorrhages, schizophrenia, mania, dementia, paranoia, obsessive compulsive disorder, depression, panic disorder, learning disabilities, ALS, psychoses, autism, and altered behaviors, including disorders in feeding, sleep patterns, balance, and perception. In addition, elevated expression of this gene product in regions of the brain indicates that it plays a role in normal neural function. Potentially, this gene product is involved in synapse formation, neurotransmission, learning, cognition, homeostasis, or neuronal differentiation or survival. Moreover, the gene or gene product may also play a role in the treatment and/or detection of developmental disorders associated with the developing embryo, sexually-linked disorders, or disorders of the cardiovascular system. Protein, as well as, antibodies directed against the protein may show utility as a tumor marker and/or immunotherapy targets for the above listed tissues.

Many polynucleotide sequences, such as EST sequences, are publicly available and accessible through sequence databases. Some of these sequences are related to SEQ ID NO:176 and may have been publicly available prior to conception of the present invention. Preferably, such related polynucleotides are specifically excluded from the scope of the present invention. To list every related sequence is cumbersome. Accordingly, preferably excluded from the present invention are one or more polynucleotides comprising a nucleotide sequence described by the general formula of a-b, where a is any integer between 1 to 1334 of SEQ ID NO:176, b is an integer of 15 to 1348, where both a and b correspond to the positions of nucleotide residues shown in SEQ ID NO:176, and where b is greater than or equal to a + 14.

FEATURES OF PROTEIN ENCODED BY GENE NO: 167

In specific embodiments, polypeptides of the invention comprise, or alternatively consists of, the following amino acid sequence: MKLLICGNYLAPSHSESSRRCCLLCFYPLCLEINFGMKVFLSMPFLVLFQSLIQED (SEQ ID NO:1099). Moreover, fragments and variants of this polypeptide (such as, for example, fragments as described herein, polypeptides at least 80%, 85%, 90%, 95%, 96%, 97%, 98%, or 99% identical to these polypeptides and polypeptides encoded by the polynucleotide which hybridize, under stringent conditions, to the polynucleotide encoding this polypeptide are encompassed by the invention. Antibodies that bind polypeptides of the invention are also encompassed by the invention. Polynucleotides encoding this polypeptide are also encompassed by the invention.

The gene encoding the disclosed cDNA is believed to reside on chromosome 15. Accordingly, polynucleotides related to this invention are useful as a marker in linkage analysis for chromosome 15.

This gene is expressed primarily in human testes tumor, and to a lesser extent, in normal human testes.

Polynucleotides and polypeptides of the invention are useful as reagents for differential identification of the tissue(s) or cell type(s) present in a biological sample and for diagnosis of diseases and conditions which include, but are not limited to, diseases of the testes, particularly cancer, and other reproductive disorders. Similarly, polypeptides and antibodies directed to these polypeptides are useful in providing immunological probes for differential identification of the tissue(s) or cell type(s). For a number of disorders of the above tissues or cells, particularly of the male reproductive tissues, expression of this gene at significantly higher or lower levels may be routinely detected in certain tissues or cell types (e.g., reproductive, testicular, and cancerous and wounded tissues) or bodily fluids (e.g., lymph, serum, seminal fluid, plasma, urine, synovial fluid and spinal fluid) or another tissue or cell sample taken from an individual having such a disorder, relative to the standard gene

expression level, i.e., the expression level in healthy tissue or bodily fluid from an individual not having the disorder.

The tissue distribution in human testicular tissue indicates that the protein products of this gene are useful for the treatment/diagnosis of reproductive diseases including cancers. Moreover, the protein may possibly have utility as a contraceptive or may be used to ameliorate disorders related to aberrant male secondary characteristics (e.g. hair, etc.). Protein, as well as, antibodies directed against the protein may, show utility as a tumor marker and/or immunotherapy targets for the above listed tissues.

Many polynucleotide sequences, such as EST sequences, are publicly available and accessible through sequence databases. Some of these sequences are related to SEQ ID NO:177 and may have been publicly available prior to conception of the present invention. Preferably, such related polynucleotides are specifically excluded from the scope of the present invention. To list every related sequence is cumbersome. Accordingly, preferably excluded from the present invention are one or more polynucleotides comprising a nucleotide sequence described by the general formula of a-b, where a is any integer between 1 to 1488 of SEQ ID NO:177, b is an integer of 15 to 1502, where both a and b correspond to the positions of nucleotide residues shown in SEQ ID NO:177, and where b is greater than or equal to a + 14.

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FEATURES OF PROTEIN ENCODED BY GENE NO: 168

The translation product of this gene was found to have homology to the gar2 gene product of Schizosaccharomyces pombe, which is thought to be involved in protein metabolism (See Genbank Accession No. gi|663262).

In specific embodiments, polypeptides of the invention comprise, or alternatively consist of, the following amino acid sequences: FSSPQGLKFRSKSSLANYLHKNGETSLKPEDFDFTVLSKRGIKSRYKDCS (SEQ ID NO:1100), ELLCYICWKNTGLFSFFLSVFRGMVSSVKSFLVGEQLLSISEPRFKMSVCKCSF LSTTSTFVPISSDSKKVSSYFSLCSESLAEQNLFMMPEVFCSEQKFDPELNDLSF

FFTRLFSSLVTLRVSPHAPASEMQTVLS (SEQ ID NO:1101), and/or TFVPISSDSKKVSSYFSLCSESLAEQNLFMMPEVFC (SEQ ID NO:1102). Moreover, fragments and variants of these polypeptides (such as, for example, fragments as described herein, polypeptides at least 80%, 85%, 90%, 95%, 96%, 97%, 98%, or 99% identical to these polypeptides and polypeptides encoded by the polynucleotide which hybridizes, under stringent conditions, to the polynucleotide encoding these polypeptides) are encompassed by the invention. Antibodies that bind polypeptides of the invention are also encompassed by the invention. Polynucleotides encoding these polypeptides are also encompassed by the invention.

The gene encoding the disclosed cDNA is believed to reside on chromosome 3. Accordingly, polynucleotides related to this invention are useful as a marker in linkage analysis for chromosome 3.

This gene is expressed primarily in fetal liver.

Polynucleotides and polypeptides of the invention are useful as reagents for differential identification of the tissue(s) or cell type(s) present in a biological sample and for diagnosis of diseases and conditions which include, but are not limited to, hepatic disorders, in addition to conditions affecting hematopoietic development and metabolic diseases. Similarly, polypeptides and antibodies directed to these polypeptides are useful in providing immunological probes for differential identification of the tissue(s) or cell type(s). For a number of disorders of the above tissues or cells, particularly of the hepatic system, and fetal hematopoietic system, expression of this gene at significantly higher or lower levels may be routinely detected in certain tissues or cell types (e.g., hepatic, metabolic, hematopoietic, and cancerous and wounded tissues) or bodily fluids (e.g., lymph, serum, bile, plasma, urine, synovial fluid and spinal fluid) or another tissue or cell sample taken from an individual having such a disorder, relative to the standard gene expression level, i.e., the expression level in healthy tissue or bodily fluid from an individual not having the disorder.

Predicted epitopes include those comprising a sequence shown in SEQ ID NO: 416 as residues: His-7 to Trp-17, Leu-19 to Lys-27, Pro-33 to Gly-44, Lys-68 to Gly-74, Lys-85 to Cys-95.

The tissue distribution in liver, combined with the homology to the gar2 protein, indicates that the protein products of this gene are useful for the treatment/diagnosis of diseases of the developing liver and hematopoietic system, and act as a growth differentiation factor for hematopoietic stem cells. Moreover, the protein product of this gene is useful for the detection and treatment of liver disorders and cancers (e.g. hepatoblastoma, jaundice, hepatitis, liver metabolic diseases and conditions that are attributable to the differentiation of hepatocyte progenitor cells). In addition, the expression in fetus would suggest a useful role for the protein product in developmental abnormalities, fetal deficiencies, pre-natal disorders, and various would-healing models and/or tissue trauma. Protein, as well as, antibodies directed against the protein may show utility as a tumor marker and/or immunotherapy targets for the above listed tissues.

Many polynucleotide sequences, such as EST sequences, are publicly available and accessible through sequence databases. Some of these sequences are related to SEQ ID NO:178 and may have been publicly available prior to conception of the present invention. Preferably, such related polynucleotides are specifically excluded from the scope of the present invention. To list every related sequence is cumbersome. Accordingly, preferably excluded from the present invention are one or more polynucleotides comprising a nucleotide sequence described by the general formula of a-b, where a is any integer between 1 to 1623 of SEQ ID NO:178, b is an integer of 15 to 1637, where both a and b correspond to the positions of nucleotide residues shown in SEQ ID NO:178, and where b is greater than or equal to a + 14.

FEATURES OF PROTEIN ENCODED BY GENE NO: 169

The polypeptide encoded by this gene is believed to be a membrane bound receptor.

Additionally, the extracellular domain of this polypeptide is expected to comprise the following amino acid sequence:

RILLVKYSANEENKYDYLPTTVNVCSELVKLVFCVLVSFCVIKKDHQSRNLK
YASWKEFSDFMKWSIPAFLYFLDNLIVFYVLSYLQPAMAVIFSNFSIITTALLF

RIVLKXRLNWIQWASLLTLFLSIVALTAGTKTLQHNLAGRGFHHDAFFSPSNS CLLFRNECPRKDNCTAKEWTFPEAKWNTTARVFSHIRLGMGHVLIIVQCFISS MANIYNEKILKEGNQLTEXIFIQNSKLYFFGILFNGLTLGLQRSNRDQIKNCGF FYGHS (SEQ ID NO:1103), TVNVCSELVKLVFCVLVSFCVIKKDHQSRN (SEQ ID NO:1104), LIVFYVLSYLQPAMAVIFSNFSIITTALLFR (SEQ ID NO:1105), FFSP SNSCLLFRNECPRKDNCTAKEWT (SEQ ID NO:1106), and/or YFFGILFNGLTL GLQRSNRDQIKNCGFF (SEQ ID NO:1107). Accordingly, preferred polypeptides encoded by this gene comprise the extracellular domain, as shown above. It will be recognized, however, that deletions of either end of the extracellular domain up to the first cysteine from the N-terminus and the first cysteine of the C-terminus, is expected to retain the biological functions of the full-length extracellular domain, because the cysteines are thought to be responsible for providing secondary structure to the molecule. Thus, deletions of one or more amino acids from either end (or both ends) of the extracellular domain are contemplated. Of course, further deletions including the cysteines are also contemplated as useful, as such polypeptides is expected to have immunological properties such as the ability to evoke an immune response. Polynucleotides encoding all of the foregoing polypeptides also encompassed by the invention.

This gene is expressed primarily in human osteoclastoma, and to a lesser extent, in hippocampus and chondrosarcoma.

Polynucleotides and polypeptides of the invention are useful as reagents for differential identification of the tissue(s) or cell type(s) present in a biological sample and for diagnosis of diseases and conditions which include, but are not limited to, skeletal or connective tissue disorders, particularly cancers. Similarly, polypeptides and antibodies directed to these polypeptides are useful in providing immunological probes for differential identification of the tissue(s) or cell type(s). For a number of disorders of the above tissues or cells, particularly of the skeletal system, expression of this gene at significantly higher or lower levels may be routinely detected in certain tissues or cell types (e.g., skeletal, neural, immune, connective, and cancerous and wounded tissues) or bodily fluids (e.g., lymph, serum, plasma, urine, synovial fluid and spinal fluid) or another tissue or cell sample taken from an individual having such

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a disorder, relative to the standard gene expression level, i.e., the expression level in healthy tissue or bodily fluid from an individual not having the disorder.

Predicted epitopes include those comprising a sequence shown in SEQ ID NO: 417 as residues: Met-1 to Cys-6, Ala-41 to Tyr-49, Lys-76 to Lys-84.

The tissue distribution in osteoclastoma and chondrosarcoma indicates that the protein products of this gene are useful for the diagnosis of cancers of the bone and connective tissues, and may act as growth factors for cells involved in bone or connective tissue growth. Moreover, this gene product may show utility in the detection and treatment of disorders and conditions affecting the skeletal system, in particular osteoporosis, bone cancer, as well as, disorders afflicting connective tissues (e.g. arthritis, trauma, tendonitis, chrondomalacia and inflammation), such as in the diagnosis or treatment of various autoimmune disorders such as rheumatoid arthritis, lupus, scleroderma, and dermatomyositis, as well as dwarfism, spinal deformation, and specific joint abnormalities as well as chondrodysplasias (i.e. spondyloepiphyseal dysplasia congenita, familial osteoarthritis, Atelosteogenesis type II, metaphyseal chondrodysplasia type Schmid). Protein, as well as, antibodies directed against the protein may show utility as a tumor marker and/or immunotherapy targets for the above listed tissues.

Many polynucleotide sequences, such as EST sequences, are publicly available and accessible through sequence databases. Some of these sequences are related to SEQ ID NO:179 and may have been publicly available prior to conception of the present invention. Preferably, such related polynucleotides are specifically excluded from the scope of the present invention. To list every related sequence is cumbersome. Accordingly, preferably excluded from the present invention are one or more polynucleotides comprising a nucleotide sequence described by the general formula of a-b, where a is any integer between 1 to 2897 of SEQ ID NO:179, b is an integer of 15 to 2911, where both a and b correspond to the positions of nucleotide residues shown in SEQ ID NO:179, and where b is greater than or equal to a + 14.

FEATURES OF PROTEIN ENCODED BY GENE NO: 170

In specific embodiments, polypeptides of the invention comprise, or alternatively consists of, an amino acid sequence selected from the group: NSVPNLQTLAVLTEAIGPEPAIPRXPREPPVATSTPATPSAGPQPLPTGTVLVPG GPAPPCLGEAWALLLPPCRPSLTSCFWSPRPSPWKETGV (SEQ ID NO:1108), VTAGRVGGGGPMPPQGKVGQDPQGPARSRLGGAGARQRVWQVWTWQ QAAPGGXGGWRALGQWPQ (SEQ ID NO:1109), STPATPSAGPQPLPTGTVLVPGGPAP (SEQ ID NO:1110), and/or QDPQGPARSRLGGAGARQR (SEQ ID NO:1111). Moreover, fragments and variants of these polypeptides (such as, for example, fragments as described herein, polypeptides at least 80%, 85%, 90%, 95%, 96%, 97%, 98%, or 99% identical to these polypeptides and polypeptides encoded by the polynucleotide which hybridizes, under stringent conditions, to the polynucleotide encoding these polypeptides) are encompassed by the invention. Antibodies that bind polypeptides of the invention are also encompassed by the invention. Polynucleotides encoding these polypeptides are also encompassed by the invention.

This gene is expressed primarily in hematopoietic progenitor cells.

Polynucleotides and polypeptides of the invention are useful as reagents for differential identification of the tissue(s) or cell type(s) present in a biological sample and for diagnosis of diseases and conditions which include, but are not limited to, hematopoietic or immune disorders, particularly cancer and autoimmune disorders. Similarly, polypeptides and antibodies directed to these polypeptides are useful in providing immunological probes for differential identification of the tissue(s) or cell type(s). For a number of disorders of the above tissues or cells, particularly of the blood/circulatory system, expression of this gene at significantly higher or lower levels may be routinely detected in certain tissues or cell types (e.g., hematopoietic, immune, and cancerous and wounded tissues) or bodily fluids (e.g., lymph, serum, plasma, urine, synovial fluid and spinal fluid) or another tissue or cell sample taken from an individual having such a disorder, relative to the standard gene expression level, i.e., the expression level in healthy tissue or bodily fluid from an individual not having the disorder.

Predicted epitopes include those comprising a sequence shown in SEQ ID NO: 418 as residues: Gln-4 to His-10, Pro-25 to His-32.

The tissue distribution in hematopoietic progenitor cells indicates that the protein products of this gene are useful for diagnosis of diseases involving growth differentiation of hematopoietic cells. Moreover, the protein product of this gene is useful for the treatment and diagnosis of hematopoetic related disorders such as anemia, pancytopenia, leukopenia, thrombocytopenia or leukemia since stromal cells are important in the production of cells of hematopoietic lineages. The uses include bone marrow cell ex vivo culture, bone marrow transplantation, bone marrow reconstitution, radiotherapy or chemotherapy of neoplasia. The gene product may also be involved in lymphopoiesis, therefore, it can be used in immune disorders such as infection, inflammation, allergy, immunodeficiency etc. In addition, this gene product may have commercial utility in the expansion of stem cells and committed progenitors of various blood lineages, and in the differentiation and/or proliferation of various cell types. Protein, as well as, antibodies directed against the protein may show utility as a tumor marker and/or immunotherapy targets for the above listed tissues.

Many polynucleotide sequences, such as EST sequences, are publicly available and accessible through sequence databases. Some of these sequences are related to SEQ ID NO:180 and may have been publicly available prior to conception of the present invention. Preferably, such related polynucleotides are specifically excluded from the scope of the present invention. To list every related sequence is cumbersome. Accordingly, preferably excluded from the present invention are one or more polynucleotides comprising a nucleotide sequence described by the general formula of a-b, where a is any integer between 1 to 505 of SEQ ID NO:180, b is an integer of 15 to 519, where both a and b correspond to the positions of nucleotide residues shown in SEQ ID NO:180, and where b is greater than or equal to a + 14.

FEATURES OF PROTEIN ENCODED BY GENE NO: 171

In specific embodiments, polypeptides of the invention comprise, or alternatively consists of, an amino acid sequence selected from the group: ALQLAFYPDAVEEWLEENVHPSLQRLQXLLQDLSEVSAPP (SEQ ID

NO:1112), CHPPALAGTLLRTPEGRAHARGLLLEAGGA (SEQ ID NO:1113), GSSSTRSWFSTSSPQRSASWHSGAPSCRSWRLPCSWLSTRMPWRSGWRKTCT PACSGCK (SEQ ID NO: 1114), ASTLQPSLSPSSPPLXPPVETAVXSRALRREGAGSFPGSNILALVTQVSLHLRSS VDALLEGNRYVTGWFSPYHRQRKLIHPV (SEQ ID NO:1115), PLGPEKAGLAXPLVXHAARPCPSTSLQSQCSPSLXXEPXXPPRSXVISGGFDE DVKAKVENLLGISSLEKTDPVRQAPCSPPCPLLPLPFXRPWRQLFSAGLSAGR GPAPSLAATSLPLSHKSASICAALWMRCWRATGMSLAGSAPTTASGSSSTRS WFSTSSPQRSASWHSGAPSCRSWRLPCSWLSTRMPWRSGWRKTCTPACSGC KLCCRTSARCLPPRCHPPALAGTLLRTPEGRAHARGLLLEAGGALXXXXAW AIRPTWASCPLAQQCLAHTQFLRALGSPWGRD (SEQ ID NO:1116), FQEDLMKMLKRKWRTFSGFPAWKKRTLLGKHPAALPVPFFPSPSPARGDSCX QQGSPQGGGRLLPWQQHPCPCHTSQPPSAQLCGCAAGGQQVCHWLVQPLPP PAEAHPPGHGSAHPARSAQPPGTVEHPRAGAGGCPAAGFLPGCRGGVAGGK RAPQPAAAAXSAAGPQRGVCPPAATHQPWQGRCSGPLRGELMPGGSCWRL GGLCXXXWPGQYGPRGRRALWPSSVLPTLSS (SEQ ID NO:1117), ALPSGVLSNVPARAGGWQRGGRHLAEVLQQSLQPLQAGVHVFLQPLLHGIR VESQLQGSLQLLHEGAPLCQEAERCGLDVLNHDRVDELPLAVVGAEPASDIP VALQQRIHRAAQMEADLCDKGKDVAAREGAGPLPAESPAENSCLHGRXKGR GRRGQGGLQGACLTGSVFSRLEIPRRFSTFALTSSSNPPEITXXRGGXXGSXXR EGLHWDCRLVLGHGRAAWXTNGQANPAFSGPKG (SEQ ID NO:1118), RQLFSAGLSAGRGPAPSLAATSLPLSHKS (SEQ ID NO:1119), ELPLAVVGAEPASDIPVALQQRIHRAAQ (SEQ ID NO:1120), and/or QPPGTVEHPRAGAGGCPAAGFLPGCRG (SEQ ID NO:1121). Moreover, fragments and variants of these polypeptides (such as, for example, fragments as described herein, polypeptides at least 80%, 85%, 90%, 95%, 96%, 97%, 98%, or 99% identical to these polypeptides and polypeptides encoded by the polynucleotide which hybridizes, under stringent conditions, to the polynucleotide encoding these polypeptides) are encompassed by the invention. Antibodies that bind polypeptides of the invention are also encompassed by the invention. Polynucleotides encoding these polypeptides are also encompassed by the invention.

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The protein product of this gene shares sequence homology with metallothionines. Thus, polypeptides encoded by this gene are expected to have metallothionine activity. Furthermore, such activities are known in the art and described elsewhere herein.

This gene is expressed primarily in kidney cortex.

Polynucleotides and polypeptides of the invention are useful as reagents for differential identification of the tissue(s) or cell type(s) present in a biological sample and for diagnosis of diseases and conditions which include, but are not limited to, renal disorders, particularly diseases of the kidney including cancer and renal dysfunction. Similarly, polypeptides and antibodies directed to these polypeptides are useful in providing immunological probes for differential identification of the tissue(s) or cell type(s). For a number of disorders of the above tissues or cells, particularly of the renal system, expression of this gene at significantly higher or lower levels may be routinely detected in certain tissues or cell types (e.g., renal, urogenital, and cancerous and wounded tissues) or bodily fluids (e.g., lymph, serum, plasma, urine, synovial fluid and spinal fluid) or another tissue or cell sample taken from an individual having such a disorder, relative to the standard gene expression level, i.e., the expression level in healthy tissue or bodily fluid from an individual not having the disorder.

Predicted epitopes include those comprising a sequence shown in SEQ ID NO: 419 as residues: Ser-47 to Gln-52.

The tissue distribution in kidney cortex indicates that the protein product of this gene is useful for the treatment/diagnosis of diseases of the kidney, including kidney failure. Moreover, this gene or gene product could be used in the treatment and/or detection of kidney diseases including nephritus, renal tubular acidosis, proteinuria, pyuria, edema, pyelonephritis, hydronephritis, nephrotic syndrome, crush syndrome, glomerulonephritis, hematuria, renal colic and kidney stones, in addition to Wilms Tumor Disease, and congenital kidney abnormalities such as horseshoe kidney, polycystic kidney, and Falconi's syndrome. Protein, as well as, antibodies directed against the protein may show utility as a tumor marker and/or immunotherapy targets for the above listed tissues.

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Many polynucleotide sequences, such as EST sequences, are publicly available and accessible through sequence databases. Some of these sequences are related to SEQ ID NO:181 and may have been publicly available prior to conception of the present invention. Preferably, such related polynucleotides are specifically excluded from the scope of the present invention. To list every related sequence is cumbersome. Accordingly, preferably excluded from the present invention are one or more polynucleotides comprising a nucleotide sequence described by the general formula of a-b, where a is any integer between 1 to 954 of SEQ ID NO:181, b is an integer of 15 to 968, where both a and b correspond to the positions of nucleotide residues shown in SEQ ID NO:181, and where b is greater than or equal to a + 14.

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FEATURES OF PROTEIN ENCODED BY GENE NO: 172

In specific embodiments, polypeptides of the invention comprise, or alternatively consist of, the following amino acid sequences: SVFERTNEFRDVLWSSI (SEQ ID NO:1122), GVVQVTFMSSVSRVTWGCQPSICPGAPPAAALAGGLRLLFERELFGLPVSSPL ICSFLEHHPRTSPPPSDCELLEGRSCVLLFIFLSPEPCTDPGMW (SEQ ID NO:1123), SKQIHSFVHSFIHLFNTHLLSTYHIPGSVQGSGDRKMNRRTQLLPSRSSQSDGG GDVLGWCSKKEQIRGEETGRPNSSLSKRSLRPPARAAAGGAPGQMLG (SEQ ID NO:1124), VTWGCQPSICPGAPPAAALAGGLRLLFE (SEQ ID NO:1125). and/or EQIRGEETGRPNSSLSKRSLRPP (SEQ ID NO:1126). Moreover, fragments and variants of these polypeptides (such as, for example, fragments as described herein, polypeptides at least 80%, 85%, 90%, 95%, 96%, 97%, 98%, or 99% identical to these polypeptides and polypeptides encoded by the polynucleotide which hybridizes, under stringent conditions, to the polynucleotide encoding these polypeptides) are encompassed by the invention. Antibodies that bind polypeptides of the invention are also encompassed by the invention. Polynucleotides encoding these polypeptides are also encompassed by the invention.

This gene is expressed primarily in 12 week old early stage human.

Polynucleotides and polypeptides of the invention are useful as reagents for differential identification of the tissue(s) or cell type(s) present in a biological sample and for diagnosis of diseases and conditions which include, but are not limited to, developmental abnormalities. Similarly, polypeptides and antibodies directed to these polypeptides are useful in providing immunological probes for differential identification of the tissue(s) or cell type(s). For a number of disorders of the above tissues or cells, particularly of the developing embryo, expression of this gene at significantly higher or lower levels may be routinely detected in certain tissues or cell types (e.g., developmental, and cancerous and wounded tissues) or bodily fluids (e.g., lymph, amniotic fluid, serum, plasma, urine, synovial fluid and spinal fluid) or another tissue or cell sample taken from an individual having such a disorder, relative to the standard gene expression level, i.e., the expression level in healthy tissue or bodily fluid from an individual not having the disorder.

Predicted epitopes include those comprising a sequence shown in SEQ ID NO: 420 as residues: Gln-31 to Thr-43, Gly-51 to Ser-58, Pro-65 to Pro-72.

The tissue distribution in embryonic tissue indicates that the protein product of this gene is useful for treatment/diagnosis of developmental conditions. The gene may be involved in vital organ development in the early stage, especially hematopoiesis, the cardiovascular system, and neural development. Moreover, expression within embryonic tissue indicates that this protein may play a role in the regulation of cellular division, and may show utility in the diagnosis and treatment of cancer and other proliferative disorders. Similarly, developmental tissues rely on decisions involving cell differentiation and/or apoptosis in pattern formation. Thus this protein may also be involved in apoptosis or tissue differentiation and could again be useful in cancer therapy. Protein, as well as, antibodies directed against the protein may show utility as a tumor marker and/or immunotherapy targets for the above listed tissues.

Many polynucleotide sequences, such as EST sequences, are publicly available and accessible through sequence databases. Some of these sequences are related to SEQ ID NO:182 and may have been publicly available prior to conception of the present invention. Preferably, such related polynucleotides are specifically excluded from the scope of the present invention. To list every related sequence is

cumbersome. Accordingly, preferably excluded from the present invention are one or more polynucleotides comprising a nucleotide sequence described by the general formula of a-b, where a is any integer between 1 to 1114 of SEQ ID NO:182, b is an integer of 15 to 1128, where both a and b correspond to the positions of nucleotide residues shown in SEQ ID NO:182, and where b is greater than or equal to a + 14.

FEATURES OF PROTEIN ENCODED BY GENE NO: 173

The translation product of this gene shares sequence homology with TGN38, an integral membrane protein previously shown to be predominantly localized to the trans-Golgi network (TGN) of cells. The gene encoding the disclosed cDNA is believed to reside on chromosome 5. Accordingly, polynucleotides related to this invention are useful as a marker in linkage analysis for chromosome 5.

This gene is expressed primarily in developing embryo, and to a lesser extent, in cancer tissues including lymphoma, endometrial, prostate and colon.

Polynucleotides and polypeptides of the invention are useful as reagents for differential identification of the tissue(s) or cell type(s) present in a biological sample and for diagnosis of diseases and conditions which include, but are not limited to, developmental abnormalities and cancer. Similarly, polypeptides and antibodies directed to these polypeptides are useful in providing immunological probes for differential identification of the tissue(s) or cell type(s). For a number of disorders of the above tissues or cells, particularly of the developing fetus, expression of this gene at significantly higher or lower levels may be routinely detected in certain tissues or cell types (e.g., developmental, reproductive, immune, gastrointestinal, and cancerous and wounded tissues) or bodily fluids (e.g., lymph, amniotic fluid, seminal fluid, serum, plasma, urine, synovial fluid and spinal fluid) or another tissue or cell sample taken from an individual having such a disorder, relative to the standard gene expression level, i.e., the expression level in healthy tissue or bodily fluid from an individual not having the disorder.

Predicted epitopes include those comprising a sequence shown in SEQ ID NO: 421 as residues: His-65 to Ser-72, Pro-82 to Gly-91, Pro-98 to Glu-118, Ser-126 to Gly-166, Pro-180 to Asp-188, Tyr-209 to Lys-214, Gln-220 to Leu-228.

The tissue distribution in the embryo, combined with the homology to an integral membrane protein indicates that the protein product of this gene is useful for the diagnosis of cancers and developmental abnormalities where aberrant expression relates to an abnormality. Expression within embryonic tissue and other cellular sources marked by proliferating cells indicates that this protein may play a role in the regulation of cellular division, and may show utility in the diagnosis and treatment of cancer and other proliferative disorders. Similarly, developmental tissues rely on decisions involving cell differentiation and/or apoptosis in pattern formation. Thus this protein may also be involved in apoptosis or tissue differentiation and could again be useful in cancer therapy. Protein, as well as, antibodies directed against the protein may show utility as a tumor marker and/or immunotherapy targets for the above listed tissues.

Many polynucleotide sequences, such as EST sequences, are publicly available and accessible through sequence databases. Some of these sequences are related to SEQ ID NO:183 and may have been publicly available prior to conception of the present invention. Preferably, such related polynucleotides are specifically excluded from the scope of the present invention. To list every related sequence is cumbersome. Accordingly, preferably excluded from the present invention are one or more polynucleotides comprising a nucleotide sequence described by the general formula of a-b, where a is any integer between 1 to 2262 of SEQ ID NO:183, b is an integer of 15 to 2276, where both a and b correspond to the positions of nucleotide residues shown in SEQ ID NO:183, and where b is greater than or equal to a + 14.

FEATURES OF PROTEIN ENCODED BY GENE NO: 174

The translation product of this gene shares sequence homology with a dnaJ heat shock protein from E. coli which is allelic to sec63, a gene that affects transit of nascent secretory proteins across the endoplasmic reticulum in yeast.

In specific embodiments, polypeptides of the invention comprise, or alternatively consist of, the following amino acid sequences: QWEHLLLLPHLLRGAHRDPGDILPLAPRSECRANSIKEYQKSIWKVYVVRLRL LKPQPNIIPTVKKIVLLAGWALFLFLAYKVSKTDREYQEYNPYEVLNLDPGAT VAEIKKQYRLLSLKYHPDKGGDEV (SEQ ID NO:1127), EERGGGGGAMAGQQFQYDDSGNTFFYFLTSFVGLIVIPATYYLWPRDQNAEQ IRLKNIRKVYGRC (SEQ ID NO:1128), RLYTGCVIFDLVSNRALSFRCMLCCNSCHSASSSLFCFSSCSLSESLSLPSSFSL WESLLVSSSSESLPLSETSSSSSFTAASFPTTPFACFCFCCFDCGNSTGVGFFFK GFFFFDLAVFLGPLLFCCHPPFVLFLLVSPCPSSAGCSSAAQMDCSFSNTSAIV CLVNLTNTVTKDPTVMLLLSSSSNTCDFISMVTYGKLPRTAITSSYFSSSRKCS RV (SEQ ID NO:1129), YQKSIWKVYVVRLRLLKPQPNIIPTVKKIVLLAGW (SEQ ID NO:1130), and/or CHPPFVLFLLVSPCPSSAGCSSAAQMDCSFSNTSA (SEQ ID NO:1131). Moreover, fragments and variants of these polypeptides (such as, for example, fragments as described herein, polypeptides at least 80%, 85%, 90%, 95%, 96%, 97%, 98%, or 99% identical to these polypeptides and polypeptides encoded by the polynucleotide which hybridizes, under stringent conditions, to the polynucleotide encoding these polypeptides) are encompassed by the invention. Antibodies that bind polypeptides of the invention are also encompassed by the invention. Polynucleotides encoding these polypeptides are also encompassed by the invention.

This gene is expressed primarily in Hodgkin's lymphoma, and to a lesser extent, in testes.

Polynucleotides and polypeptides of the invention are useful as reagents for differential identification of the tissue(s) or cell type(s) present in a biological sample and for diagnosis of diseases and conditions which include, but are not limited to, immune or hematopoietic disorders, particularly cancer. Similarly, polypeptides and antibodies directed to these polypeptides are useful in providing immunological probes for differential identification of the tissue(s) or cell type(s). For a number of disorders of the above tissues or cells, particularly of the immune system, expression of this gene at significantly higher or lower levels may be routinely detected in certain tissues or cell types (e.g., immune, hematopoietic, reproductive, testicular, and

cancerous and wounded tissues) or bodily fluids (e.g., lymph, seminal fluid, serum, plasma, urine, synovial fluid and spinal fluid) or another tissue or cell sample taken from an individual having such a disorder, relative to the standard gene expression level, i.e., the expression level in healthy tissue or bodily fluid from an individual not having the disorder.

Predicted epitopes include those comprising a sequence shown in SEQ ID NO: 422 as residues: Val-37 to Pro-49, His-76 to Asp-82, Thr-97 to Trp-105, Arg-158 to Asp-165, Glu-199 to Asp-214, Asn-229 to Pro-236, Thr-261 to Gln-266, Arg-292 to Glu-298, Glu-335 to Lys-351, Glu-372 to Glu-377, Leu-398 to Asn-405, Glu-437 to Pro-480, Gln-487 to Gln-495, Lys-507 to Ala-555, Ser-563 to Arg-569, Pro-588 to Glu-593, Lys-618 to Val-623, Pro-630 to Asn-635, Ser-644 to Gly-649, Lys-664 to Trp-673, Gly-679 to Phe-689, Asp-691 to Asp-704.

The tissue distribution in Hodgkin's lymphoma, combined with the homology to dnaJ and sec63 indicates that the protein product of this gene is useful as a diagnostic for cancer, that the protein may be useful in regulating gene expression levels, and that it is essential for normal protein metabolism. Therefore, protein products of this gene may show utility as an anticancer agent, or even serve to protect from viral or bacterial infections, based upon its homologous function as a protein chaperone. Protein, as well as, antibodies directed against the protein may show utility as a tumor marker and/or immunotherapy targets for the above listed tissues.

Many polynucleotide sequences, such as EST sequences, are publicly available and accessible through sequence databases. Some of these sequences are related to SEQ ID NO:184 and may have been publicly available prior to conception of the present invention. Preferably, such related polynucleotides are specifically excluded from the scope of the present invention. To list every related sequence is cumbersome. Accordingly, preferably excluded from the present invention are one or more polynucleotides comprising a nucleotide sequence described by the general formula of a-b, where a is any integer between 1 to 3360 of SEQ ID NO:184, b is an integer of 15 to 3374, where both a and b correspond to the positions of nucleotide residues shown in SEQ ID NO:184, and where b is greater than or equal to a + 14.

FEATURES OF PROTEIN ENCODED BY GENE NO: 175

The gene encoding the disclosed cDNA is believed to reside on chromosome 5. Accordingly, polynucleotides related to this invention are useful as a marker in linkage analysis for chromosome 5. Contact of cells with supernatant expressing the product of this gene has been shown to increase the permeability of the plasma membrane of chondrocytes to calcium. Thus it is likely that the product of this gene is involved in a signal transduction pathway that is initiated when the product binds a receptor on the surface of the plasma membrane of both chondrocytes , in addition to other cell-lines or tissue cell types. Thus, polynucleotides and polypeptides have uses which include, but are not limited to, activating chondrocytes.

This gene is expressed primarily in endothelial cells, and to a lesser extent, in bone marrow stromal cells.

Polynucleotides and polypeptides of the invention are useful as reagents for differential identification of the tissue(s) or cell type(s) present in a biological sample and for diagnosis of diseases and conditions which include, but are not limited to, immune, hematopoietic, endothelial, or vascular disorders, such as diseases involving angiogenic abnormalities including diabetic retinopathy, macular degeneration, and other diseases including arteriosclerosis and cancer. Similarly, polypeptides and antibodies directed to these polypeptides are useful in providing immunological probes for differential identification of the tissue(s) or cell type(s). For a number of disorders of the above tissues or cells, particularly of the vascular system, expression of this gene at significantly higher or lower levels may be routinely detected in certain tissues or cell types (e.g., immune, hematopoietic, endothelial, vascular, and cancerous and wounded tissues) or bodily fluids (e.g., lymph, serum, plasma, urine, synovial fluid and spinal fluid) or another tissue or cell sample taken from an individual having such a disorder, relative to the standard gene expression level, i.e., the expression level in healthy tissue or bodily fluid from an individual not having the disorder.

The tissue distribution in endothelial cells indicates that the protein products of this gene are useful for treating diseases where an increase or decrease in angiogenesis is indicated and as a factor in the wound healing process. In addition,

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the protein product of this gene may show utility in the treatment, detection, and/or prevention of a variety of vascular disorders, which include, but are not limited to microvascular disease, embolism, thrombosis, atherosclerosis, aneurysm, or stroke. Moreover, the protein product of this gene is useful for the treatment and diagnosis of hematopoetic related disorders such as anemia, pancytopenia, leukopenia, thrombocytopenia or leukemia since stromal cells are important in the production of cells of hematopoietic lineages. The uses include bone marrow cell ex vivo culture, bone marrow transplantation, bone marrow reconstitution, radiotherapy or chemotherapy of neoplasia. The gene product may also be involved in lymphopoiesis, therefore, it can be used in immune disorders such as infection, inflammation, allergy, immunodeficiency etc. In addition, this gene product may have commercial utility in the expansion of stem cells and committed progenitors of various blood lineages, and in the differentiation and/or proliferation of various cell types. Protein, as well as, antibodies directed against the protein may show utility as a tumor marker and/or immunotherapy targets for the above listed tissues.

Many polynucleotide sequences, such as EST sequences, are publicly available and accessible through sequence databases. Some of these sequences are related to SEQ ID NO:185 and may have been publicly available prior to conception of the present invention. Preferably, such related polynucleotides are specifically excluded from the scope of the present invention. To list every related sequence is cumbersome. Accordingly, preferably excluded from the present invention are one or more polynucleotides comprising a nucleotide sequence described by the general formula of a-b, where a is any integer between 1 to 1323 of SEQ ID NO:185, b is an integer of 15 to 1337, where both a and b correspond to the positions of nucleotide residues shown in SEQ ID NO:185, and where b is greater than or equal to a + 14.

FEATURES OF PROTEIN ENCODED BY GENE NO: 176

The translation product of this gene shares sequence homology with both the RIC and MAT8 proteins (mouse), which are thought to be important in regulating

chloride conductance in cells by modulating the response mediated by cAMP and protein kinase C to extracellular signals.

In specific embodiments, polypeptides of the invention comprise, or alternatively consist of, the following amino acid sequences:

GTSLDAAATAASLSPRGCRLRTPSSD (SEQ ID NO:1132), QIQRHTRAPKQLIPLMTPRRSLRDHPQAQTSRQTPRPSSHLVFMRMTPSSMM NTPSGNGGCWSQLCCSSQASSSSPVASAGSCPGYAGIIAGESIRNRS (SEQ ID NO:1133), PRRSLRDHPQAQTSRQTPRPSSHLVFM (SEQ ID NO:1134), THPPETGAVGRSCAVHHRHHHPHQWQVQAAVPVMPESLQVSPSETGADNXL GTRRPSPLPAHRAQPPASPRRAWPEREDTDDEAGARAAGPSLLPPPTLPAPEG YLAPWGLSLKLSPLLRQKVKHCGLC (SEQ ID NO:1135), PESLQVSPSETGADNXLGTRRPSPLPAHRAQPPASP (SEQ ID NO:1136), GTAPKAPGSLQGRAGLGEVGDSDRQPWLQLHHLCLPSLARLFEGMQEAGHG ELAGGLVFGCPAGCQLLFLMDSPAMIPA (SEQ ID NO:1137), GEVGDSDRQPWLQLHHLCLPSLARLFEGMQEAGH (SEQ ID NO:1138), GSGGLSGRLCLGMVSQRASWCHQWDELLWCSCVSLDLSLEAHPFLPVAGSG SGVVVFHQQARLGLERWAGVLCRLHLGLVSGPECP (SEQ ID NO:1139), and/or QWDELLWCSCVSLDLSLEAHPFLPVAGSGSGVVVFHQQARL (SEQ ID NO:1140). Moreover, fragments and variants of these polypeptides (such as, for example, fragments as described herein, polypeptides at least 80%, 85%, 90%, 95%, 96%, 97%, 98%, or 99% identical to these polypeptides and polypeptides encoded by the polynucleotide which hybridizes, under stringent conditions, to the polynucleotide encoding these polypeptides) are encompassed by the invention. Antibodies that bind polypeptides of the invention are also encompassed by the invention. Polynucleotides encoding these polypeptides are also encompassed by the invention.

The gene encoding the disclosed cDNA is believed to reside on chromosome 19. Accordingly, polynucleotides related to this invention are useful as a marker in linkage analysis for chromosome 19.

This gene is expressed primarily in amniotic cells and hematopoietic cells including macrophages, neutrophils, T cells, TNF induced aortic endothelium, and to a lesser extent in testes, TNF induced epithelial cells, and smooth muscle.

Polynucleotides and polypeptides of the invention are useful as reagents for differential identification of the tissue(s) or cell type(s) present in a biological sample and for diagnosis of diseases and conditions which include, but are not limited to, immune or hematopoietic disorders, particularly inflammatory responses mediated by T cells, macrophages, and/or neutrophils, particularly those involving TNF, and also cancer. Similarly, polypeptides and antibodies directed to these polypeptides are useful in providing immunological probes for differential identification of the tissue(s) or cell type(s). For a number of disorders of the above tissues or cells, particularly of the immune system, expression of this gene at significantly higher or lower levels may be routinely detected in certain tissues or cell types (e.g., immune, hematopoietic, developmental, and cancerous and wounded tissues) or bodily fluids (e.g., lymph, serum, plasma, urine, synovial fluid and spinal fluid) or another tissue or cell sample taken from an individual having such a disorder, relative to the standard gene expression level, i.e., the expression level in healthy tissue or bodily fluid from an individual not having the disorder.

Predicted epitopes include those comprising a sequence shown in SEQ ID NO: 424 as residues: Thr-19 to Ala-33, Leu-54 to Asp-82, Pro-89 to Ala-97, Pro-100 to Lys-125, Ser-127 to Phe-135, Gly-164 to Leu-169, Cys-173 to Arg-178.

The tissue distribution in hematopoietic cells, combined with the homology to the RIC and mat-8 genes, indicates that the protein product of this gene is useful for modifying inflammatory responses to cytokines such as TNF, and thus modifying the duration and/or severity of inflammation. Polynucleotides and polypeptides derived from this gene are thought to be useful in the diagnosis and treatment of cancer. The protein product of this gene is useful for the treatment and diagnosis of hematopoetic related disorders such as anemia, pancytopenia, leukopenia, thrombocytopenia or leukemia, since stromal cells are important in the production of cells of hematopoietic lineages. The uses include bone marrow cell ex vivo culture, bone marrow transplantation, bone marrow reconstitution, radiotherapy or chemotherapy of neoplasia. The gene product may also be involved in lymphopoiesis, therefore, it can be used in immune disorders such as infection, inflammation, allergy, immunodeficiency etc. In addition, this gene product may have commercial utility in the expansion of stem cells and committed progenitors of various blood lineages, and

in the differentiation and/or proliferation of various cell types. Protein, as well as, antibodies directed against the protein may show utility as a tumor marker and/or immunotherapy targets for the above listed tissues.

Many polynucleotide sequences, such as EST sequences, are publicly available and accessible through sequence databases. Some of these sequences are related to SEQ ID NO:186 and may have been publicly available prior to conception of the present invention. Preferably, such related polynucleotides are specifically excluded from the scope of the present invention. To list every related sequence is cumbersome. Accordingly, preferably excluded from the present invention are one or more polynucleotides comprising a nucleotide sequence described by the general formula of a-b, where a is any integer between 1 to 927 of SEQ ID NO:186, b is an integer of 15 to 941, where both a and b correspond to the positions of nucleotide residues shown in SEQ ID NO:186, and where b is greater than or equal to a + 14.

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FEATURES OF PROTEIN ENCODED BY GENE NO: 177

This gene is expressed primarily in endothelial cells.

Polynucleotides and polypeptides of the invention are useful as reagents for differential identification of the tissue(s) or cell type(s) present in a biological sample and for diagnosis of diseases and conditions which include, but are not limited to, vascular disorders, including vascular restenosis. Similarly, polypeptides and antibodies directed to these polypeptides are useful in providing immunological probes for differential identification of the tissue(s) or cell type(s). For a number of disorders of the above tissues or cells, particularly of the vascular system, expression of this gene at significantly higher or lower levels may be routinely detected in certain tissues or cell types (e.g., vascular, endothelial, and cancerous and wounded tissues) or bodily fluids (e.g., lymph, serum, plasma, urine, synovial fluid and spinal fluid) or another tissue or cell sample taken from an individual having such a disorder, relative to the standard gene expression level, i.e., the expression level in healthy tissue or bodily fluid from an individual not having the disorder.

The tissue distribution in endothelial tissue indicates that the protein product of this gene is useful for treating diseases associated with vascular responses to injury such as vascular restenosis following angioplasty. Moreover, the protein product of this gene is useful for the treatment, detection, and/or prevention of a variety of other vascular disorders, which include, but are not limited to microvascular disease, embolism, thrombosis, atherosclerosis, aneurysm, or stroke. Protein, as well as, antibodies directed against the protein may show utility as a tumor marker and/or immunotherapy targets for the above listed tissues.

Many polynucleotide sequences, such as EST sequences, are publicly available and accessible through sequence databases. Some of these sequences are related to SEQ ID NO:187 and may have been publicly available prior to conception of the present invention. Preferably, such related polynucleotides are specifically excluded from the scope of the present invention. To list every related sequence is cumbersome. Accordingly, preferably excluded from the present invention are one or more polynucleotides comprising a nucleotide sequence described by the general formula of a-b, where a is any integer between 1 to 664 of SEQ ID NO:187, b is an integer of 15 to 678, where both a and b correspond to the positions of nucleotide residues shown in SEQ ID NO:187, and where b is greater than or equal to a + 14.

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FEATURES OF PROTEIN ENCODED BY GENE NO: 178

This gene appears to be chimeric. There are two ORFs of interest. The first ORF-1 encodes a polypeptide preferably comprising one of the following polypeptide sequences:

MRPDWKAGAGPGGPPQKPAPSSQRKPPARPSAAAAAIAVAAAEEERRLRQR NRLRLEEDKPAVERCLEELVFGDVENDEDALLRRLRGPRVQEHEDSGDSEVE NEAKGNFPPQKKPVWVDEEDEDEEMVDMMNNRFRKDMMKNASESKLSKD NLKKRLKEEFQHAMGGVPAWAETTKRKTSSDDESEEDEDDLLQRTGNFISTS TSLPRGILKMKNCQHANAERPTVARISICAVPSRCTDCDGCWD (SEQ ID NO:1141); and/or

CLEELVFGDVENDEDALLRRLRGPRVQEHEDSGDSEVENEAKGNFPPQKKPV

WVDEEDEDEEMVDMMNNRFRKDMMKNASESKLSKDNLKKRLKEEFQHAM
GGVPAWAETTKRKTSSDDESEEDEDDLLQRTGNFISTSTSLPRGILKMKNCQH
ANAERPTVARISICAVPSRCTDCDGC (SEQ ID NO:1142). The second ORF (ORF-2) encodes a polypeptide preferably comprising one of the following polypeptide sequences:
LKEKIVRSFEVSPDGSFLLINGIAGYLHLLAMKTKELIGSMKINGRVAASTFSS
DSKKVYASSGDGEVYVWDVNSRKCLNRFVDEGSLYGLSIATSRNGQYVACG
SNCGVVNIYNQDSCLQETNPKPIKAIMNLVTGVTSLTFNPTTEILAIASEKMKE
AVRLVHLPSCTVFSNFPVIKNKNISHVHTMDFSPRSGYFALGNEKGKALMYR
LHHYSDF (SEQ ID NO:1143); and/or
KINGRVAASTFSSDSKKVYASSGDGEVYVWDVNSRKCLNRFVDEGSLYGLSI
ATSRNGQYVACGSNCGVVNIYNQDSCLQETNPKPIKAIMNLVTGVTSLTFNP
TTEILAIASEKMKEAVRLVHLPSCTVFSNFPVIKNKNISHVHTMDFSPRSGYFA
LGNEKGKAL (SEQ ID NO:1144).

In specific embodiments, polypeptides of the invention comprise, or alternatively consist of, the following amino acid sequences: WLLGLDNAVSLFQVDGKTNPKIQSIYLERFPIFKACFSANGEEVLATSTHSKV LYVYD (SEQ ID NO:1145), LVFGDVENDEDALLRRLRGPRVQ (SEQ ID NO:1146), KNASESKLSKDNLKKRLKEEFQHAMGGVP (SEQ ID NO:1147), and/or SLPRGILKMKNCQHANAERPTVA (SEQ ID NO:1148). Moreover, fragments and variants of these polypeptides (such as, for example, fragments as described herein, polypeptides at least 80%, 85%, 90%, 95%, 96%, 97%, 98%, or 99% identical to these polypeptides and polypeptides encoded by the polynucleotide which hybridizes, under stringent conditions, to the polynucleotide encoding these polypeptides) are encompassed by the invention. Antibodies that bind polypeptides of the invention are also encompassed by the invention. Polynucleotides encoding these polypeptides are also encompassed by the invention.

The translation product of this gene shares homology with the transcriptional repressor TUP1 of Candida albicans (See Genbank Accession No. gi|2245634 (AF005741)), which is thought to modulate the expression levels of cellular filament and may implicate this protein as serving a useful role in the amelioration of proliferating cells and tissues.

This gene is expressed primarily in epidydimus and endometrial tumors, and to a lesser extent, in T cell lymphoma and cell lines derived from colon cancer.

Polynucleotides and polypeptides of the invention are useful as reagents for differential identification of the tissue(s) or cell type(s) present in a biological sample and for diagnosis of diseases and conditions which include, but are not limited to, reproductive or developmental conditions, which include tumors of the reproductive organs, including testis and endometrial cells. Similarly, polypeptides and antibodies directed to these polypeptides are useful in providing immunological probes for differential identification of the tissue(s) or cell type(s). For a number of disorders of the above tissues or cells, particularly of the reproductive system, expression of this gene at significantly higher or lower levels may be routinely detected in certain tissues or cell types (e.g., reproductive, developmental, and cancerous and wounded tissues) or bodily fluids (e.g., lymph, amniotic fluid, seminal fluid, serum, plasma, urine, synovial fluid and spinal fluid) or another tissue or cell sample taken from an individual having such a disorder, relative to the standard gene expression level, i.e., the expression level in healthy tissue or bodily fluid from an individual not having the disorder.

Predicted epitopes include those comprising a sequence shown in SEQ ID NO: 426 as residues: Ser-67 to Lys-72, Val-87 to Leu-93, Tyr-128 to Pro-141, Asp-204 to Gly-210.

The tissue distribution in reproductive tissue cancers, combined with the homology to a transcriptional repressor protein, indicates that the protein products of this gene are useful for treating tumors of the endometrium or epithelial tumors of the reproductive system. Moreover, the protein may also be useful as a contraceptive. Protein, as well as, antibodies directed against the protein may show utility as a tumor marker and/or immunotherapy targets for the above listed tissues.

Many polynucleotide sequences, such as EST sequences, are publicly available and accessible through sequence databases. Some of these sequences are related to SEQ ID NO:188 and may have been publicly available prior to conception of the present invention. Preferably, such related polynucleotides are specifically excluded from the scope of the present invention. To list every related sequence is cumbersome. Accordingly, preferably excluded from the present invention are one or

more polynucleotides comprising a nucleotide sequence described by the general formula of a-b, where a is any integer between 1 to 1834 of SEQ ID NO:188, b is an integer of 15 to 1848, where both a and b correspond to the positions of nucleotide residues shown in SEQ ID NO:188, and where b is greater than or equal to a + 14.

FEATURES OF PROTEIN ENCODED BY GENE NO: 179

In specific embodiments, polypeptides of the invention comprise, or alternatively consists of, an amino acid sequence selected from the group: MRILQLILLALATGLVGGETRIIKGFECKLHSQPWQAALFEKTRLLCGATLIAP RWLLTAAHCLKPRYIVHLGQHNLQKEEGCEQTRTATESFPHPGFNNSLPNKD HRNDIMLVKMASPVSITWAVRPLTLSSRCVTAGTSCSFPAGAARPDPSYACLT PCDAPTSPSLSTRSVRTPTPATSQTPWCVPACRKGARTPARVTPGALWSVTSL FKALSPGARIRVRSPESLVSTRKSANMWTGSRRR (SEQ ID NO:1149); ETRIIKGFECKLHSQPWQAALFEKTRLLCGATLIAPRWLLTAAHCLKPRYIVH LGQHNLQKEEGCEQTRTATESFPHPGFNNSLPNKDHRNDIMLVKMASPVSIT WAVRPLTLSSRCVTAGTSCSFPAGAARPDPSYACLTPCDAPTSPSLSTRSVRTP TPATSQTPWCVPACRKGARTPARVTPGALWSVTSLFKALSPGARIRVRSPESL VSTRKSANMWTGSRRR (SEQ ID NO:1150); and/or CKLHSQPWQAALFEKTRLLCGATLIAPRWLLTAAHCLKPRYIVHLGQHNLQK EEGCEQTRTATESFPHPGFNNS (SEQ ID NO:1151). Moreover, fragments and variants of these polypeptides (such as, for example, fragments as described herein, polypeptides at least 80%, 85%, 90%, 95%, 96%, 97%, 98%, or 99% identical to these polypeptides and polypeptides encoded by the polynucleotide which hybridizes, under stringent conditions, to the polynucleotide encoding these polypeptides) are encompassed by the invention. Antibodies that bind polypeptides of the invention are also encompassed by the invention. Polynucleotides encoding these polypeptides are also encompassed by the invention.

The translation product of this gene shares sequence homology with neuropsin, a novel serine protease, which is thought to be important in modulating extracellular signaling pathways in the brain. Owing to the structural similarity to

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other serine proteases, the protein products of this gene are expected to have serine protease activity which may be assayed by methods known in the art and described elsewhere herein. Moreover, this protein has been shown to also have homology to PSA (prostate specific antigen). PSA is a serum marker for prostate cancer and it is a member of the kallikrein family. The members of the kallikrein family are secreted serine proteases and some of them are good tissue specific markers. This new member of the kallikrein family has been detected twice in endometrial tumor cDNA library and therefore is a good candidate as a serum marker for endometrial tumor.

This gene is expressed primarily in endometrial tumor, and to a lesser extent, in colon cancer, benign hypertrophic prostate, and thymus.

Polynucleotides and polypeptides of the invention are useful as reagents for differential identification of the tissue(s) or cell type(s) present in a biological sample and for diagnosis of diseases and conditions which include, but are not limited to, reproductive, immune, or endocrine disorders, particularly cancers of the endometrium or colon and benign hypertrophy of the prostate. Similarly, polypeptides and antibodies directed to these polypeptides are useful in providing immunological probes for differential identification of the tissue(s) or cell type(s). For a number of disorders of the above tissues or cells, particularly of the urogenital or reproductive systems, expression of this gene at significantly higher or lower levels may be routinely detected in certain tissues or cell types (e.g., reproductive, immune, endocrine, gastrointestinal, and cancerous and wounded tissues) or bodily fluids (e.g., lymph, serum, seminal fluid, plasma, urine, synovial fluid and spinal fluid) or another tissue or cell sample taken from an individual having such a disorder, relative to the standard gene expression level, i.e., the expression level in healthy tissue or bodily fluid from an individual not having the disorder.

Predicted epitopes include those comprising a sequence shown in SEQ ID NO: 427 as residues: Glu-27 to Trp-35, Leu-77 to Ala-89, Pro-96 to Asn-109, Ser-149 to Arg-156, Gln-172 to Ile-182, Glu-193 to Gly-204, Glu-245 to Asn-250.

The tissue distribution in proliferative reproductive tissues, combined with the homology to serine proteases indicates that the protein product of this gene is useful for diagnosing, treating, and/or preventing hyperproliferative disorders such as cancer of the endometrium or colon and hyperplasia of the prostate. Similarly, expression

within cellular sources marked by proliferating cells indicates that this protein may play a role in the regulation of cellular division, and may show utility in the diagnosis and treatment of cancer and other proliferative disorders. Similarly, developmental tissues rely on decisions involving cell differentiation and/or apoptosis in pattern formation. Thus this protein may also be involved in apoptosis or tissue differentiation and could again be useful in cancer therapy. Protein, as well as, antibodies directed against the protein may show utility as a tumor marker and/or immunotherapy targets for the above listed tissues.

Many polynucleotide sequences, such as EST sequences, are publicly available and accessible through sequence databases. Some of these sequences are related to SEQ ID NO:189 and may have been publicly available prior to conception of the present invention. Preferably, such related polynucleotides are specifically excluded from the scope of the present invention. To list every related sequence is cumbersome. Accordingly, preferably excluded from the present invention are one or more polynucleotides comprising a nucleotide sequence described by the general formula of a-b, where a is any integer between 1 to 1278 of SEQ ID NO:189, b is an integer of 15 to 1292, where both a and b correspond to the positions of nucleotide residues shown in SEQ ID NO:189, and where b is greater than or equal to a + 14.

FEATURES OF PROTEIN ENCODED BY GENE NO: 180

In specific embodiments, polypeptides of the invention comprise, or alternatively consists of, an amino acid sequence selected from the group: VLQGRYFSPILEMRRLRPEGXXNLPGGSRAQKEPRQDLTLVLWPHCPHFAMT RSYVPTKQCMVQGSFYCIFIFKGPVQNWC (SEQ ID NO:1152), and/or CPRRRT CVRVEKSRPFQCQLHSIS (SEQ ID NO:1153). Moreover, fragments and variants of these polypeptides (such as, for example, fragments as described herein, polypeptides at least 80%, 85%, 90%, 95%, 96%, 97%, 98%, or 99% identical to these polypeptides and polypeptides encoded by the polynucleotide which hybridizes, under stringent conditions, to the polynucleotide encoding these polypeptides) are encompassed by the invention. Antibodies that bind polypeptides of the invention are

also encompassed by the invention. Polynucleotides encoding these polypeptides are also encompassed by the invention.

This gene is expressed primarily in fetal brain.

Polynucleotides and polypeptides of the invention are useful as reagents for differential identification of the tissue(s) or cell type(s) present in a biological sample and for diagnosis of diseases and conditions which include, but are not limited to, neural disorders, particularly neurodegenerative conditions, in addition to identifying and expanding stem cells in the CNS. Similarly, polypeptides and antibodies directed to these polypeptides are useful in providing immunological probes for differential identification of the tissue(s) or cell type(s). For a number of disorders of the above tissues or cells, particularly of the nervous system, expression of this gene at significantly higher or lower levels may be routinely detected in certain tissues or cell types (e.g., neural, developmental, and cancerous and wounded tissues) or bodily fluids (e.g., lymph, amniotic fluid, serum, plasma, urine, synovial fluid and spinal fluid) or another tissue or cell sample taken from an individual having such a disorder, relative to the standard gene expression level, i.e., the expression level in healthy tissue or bodily fluid from an individual not having the disorder.

Predicted epitopes include those comprising a sequence shown in SEQ ID NO: 428 as residues: Met-1 to Lys-9, Glu-26 to Lys-37, Lys-39 to Lys-48.

The tissue distribution in fetal brain indicates that the protein products of this gene are useful for detecting and expanding stem cell populations in the (or of the) central nervous system. Moreover, the protein product of this gene is useful for the detection/treatment of neurodegenerative disease states, behavioral disorders, or inflammatory conditions which include, but are not limited to Alzheimer's Disease, Parkinson's Disease, Huntington's Disease, Tourette's Syndrome, meningitis, encephalitis, demyelinating diseases, peripheral neuropathies, neoplasia, trauma, congenital malformations, spinal cord injuries, ischemia and infarction, aneurysms, hemorrhages, schizophrenia, mania, dementia, paranoia, obsessive compulsive disorder, depression, panic disorder, learning disabilities, ALS, psychoses, autism, and altered behaviors, including disorders in feeding, sleep patterns, balance, and perception. In addition, elevated expression of this gene product in regions of the brain indicates that it plays a role in normal neural function. Potentially, this gene

product is involved in synapse formation, neurotransmission, learning, cognition, homeostasis, or neuronal differentiation or survival. Protein, as well as, antibodies directed against the protein may show utility as a tumor marker and/or immunotherapy targets for the above listed tissues.

Many polynucleotide sequences, such as EST sequences, are publicly available and accessible through sequence databases. Some of these sequences are related to SEQ ID NO:190 and may have been publicly available prior to conception of the present invention. Preferably, such related polynucleotides are specifically excluded from the scope of the present invention. To list every related sequence is cumbersome. Accordingly, preferably excluded from the present invention are one or more polynucleotides comprising a nucleotide sequence described by the general formula of a-b, where a is any integer between 1 to 892 of SEQ ID NO:190, b is an integer of 15 to 906, where both a and b correspond to the positions of nucleotide residues shown in SEQ ID NO:190, and where b is greater than or equal to a + 14.

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FEATURES OF PROTEIN ENCODED BY GENE NO: 181

In specific embodiments, polypeptides of the invention comprise, or alternatively consist of, the following amino acid sequences: PKEPGVPE (SEQ ID NO:1154), LQLKPRDPFSTLGPNAVLSPQRLVLETLSKLSIQDNNVDLILATPPFSRLEKLY STMVRFLSDRKNPVCRRWLWYCWPTWLRGTAWQLVPLQCRRAVSATSWAS (SEQ ID NO:1155), RDPFSTLGPNAVLSPQRLVLETLSKLS (SEQ ID NO:1156), EVISGLFIQSRRRERGQGVVGSHMILWGKSLFFFSPQRLTKNIFKNYSLLLTQR FLFPCETLLLQYVYSIRCTVQYMKGSTLYCTGLSSEQGLFTTANFLAPARL (SEQ ID NO:1157), and/or IRCTVQYMKGSTLYCTGLSSEQG (SEQ ID NO:1158). Moreover, fragments and variants of these polypeptides (such as, for example, fragments as described herein, polypeptides at least 80%, 85%, 90%, 95%, 96%, 97%, 98%, or 99% identical to these polypeptides and polypeptides encoded by the polynucleotide which hybridizes, under stringent conditions, to the polynucleotide encoding these polypeptides) are encompassed by the invention. Antibodies that bind

polypeptides of the invention are also encompassed by the invention. Polynucleotides encoding these polypeptides are also encompassed by the invention.

This gene is expressed primarily in early stage human brain, fetal liver/spleen, and stromal cells.

Polynucleotides and polypeptides of the invention are useful as reagents for differential identification of the tissue(s) or cell type(s) present in a biological sample and for diagnosis of diseases and conditions which include, but are not limited to, developmental abnormalities, neural, immune, or hematopoietic disorders. Similarly, polypeptides and antibodies directed to these polypeptides are useful in providing immunological probes for differential identification of the tissue(s) or cell type(s). For a number of disorders of the above tissues or cells, particularly of the central nervous system, expression of this gene at significantly higher or lower levels may be routinely detected in certain tissues or cell types (e.g., developmental, neural, immune, hematopoietic, and cancerous and wounded tissues) or bodily fluids (e.g., lymph, amniotic fluid, serum, plasma, urine, synovial fluid and spinal fluid) or another tissue or cell sample taken from an individual having such a disorder, relative to the standard gene expression level, i.e., the expression level in healthy tissue or bodily fluid from an individual not having the disorder.

Predicted epitopes include those comprising a sequence shown in SEQ ID NO: 429 as residues: Gln-42 to Gln-47, Gln-54 to Pro-60.

The tissue distribution in embryonic brain and fetal liver indicates that the protein products of this gene play a role in the development of the central nervous and hematopoietic systems. Therefore this gene and its products are useful for diagnosing or treating developmental abnormalities of the central nervous system. Moreover, the protein product of this gene is useful for the treatment and diagnosis of hematopoetic related disorders such as anemia, pancytopenia, leukopenia, thrombocytopenia or leukemia since stromal cells are important in the production of cells of hematopoietic lineages. The uses include bone marrow cell ex vivo culture, bone marrow transplantation, bone marrow reconstitution, radiotherapy or chemotherapy of neoplasia. The gene product may also be involved in lymphopoiesis, therefore, it can be used in immune disorders such as infection, inflammation, allergy, immunodeficiency etc. In addition, this gene product may have commercial utility in

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the expansion of stem cells and committed progenitors of various blood lineages, and in the differentiation and/or proliferation of various cell types. Protein, as well as, antibodies directed against the protein may show utility as a tumor marker and/or immunotherapy targets for the above listed tissues.

Many polynucleotide sequences, such as EST sequences, are publicly available and accessible through sequence databases. Some of these sequences are related to SEQ ID NO:191 and may have been publicly available prior to conception of the present invention. Preferably, such related polynucleotides are specifically excluded from the scope of the present invention. To list every related sequence is cumbersome. Accordingly, preferably excluded from the present invention are one or more polynucleotides comprising a nucleotide sequence described by the general formula of a-b, where a is any integer between 1 to 1927 of SEQ ID NO:191, b is an integer of 15 to 1941, where both a and b correspond to the positions of nucleotide residues shown in SEQ ID NO:191, and where b is greater than or equal to a + 14.

D6E3V5 = 06N04

FEATURES OF PROTEIN ENCODED BY GENE NO: 182

In specific embodiments, polypeptides of the invention comprise, or alternatively consists of, an amino acid sequence selected from the group: MPIIDQVNPELHDFMQSAEVGTIFALSWLITWFGHVLSDFRHVVRLYDFFLAC HPLMPIYFAAVIVLYREQEVLDCDCDMASVHHLLSQIPQDLPYETLISRXETFL FSFPHPNLLGRPLPNSKLRGRQPLLSKTLSWHQPSRGLIWCCGSGXRGLLRPE DRTKDVLTKPRTNRFVKLAVMGLTVALGAAALAVVKSALEWAPKFQLQLFP (SEQ ID NO:1159; "ORF-1"); or CPEFFIPATLPCPFVFAFTSEASSRAYLTQRGPGGLAQNLMPLPVGFWMGSLP PPWCWRKWVSEACSCFC (SEQ ID NO:1160; "ORF-2"). Moreover, fragments and variants of these polypeptides (such as, for example, fragments as described herein, polypeptides at least 80%, 85%, 90%, 95%, 96%, 97%, 98%, or 99% identical to these polypeptides and polypeptides encoded by the polynucleotide which hybridizes, under stringent conditions, to the polynucleotide encoding these polypeptides) are encompassed by the invention. Antibodies that bind polypeptides

of the invention are also encompassed by the invention. Polynucleotides encoding these polypeptides are also encompassed by the invention.

ORF-2 is structurally similar to various TGF-beta family members. Thus, this polypeptide is expected to have a variety of activities in the modulation of cell growth and proliferation.

In specific embodiments, polypeptides of the invention comprise, or alternatively consists of, the following amino acid sequence: CRQAGAVRGHPMFQFTFYGVTXRFPVTRAAQAQQVAKAAASFRNPLPPTPG RWQRAHPKAHWERHKILCQAPRSPLCQVGSATGL (SEQ ID NO:1161), HILNYLMPIIDQVNPELHDFMQSAEVGTIFALSWLITWFGHVLSDFRHVVRLY DFFLACHPLMPIYFAAVIVLYREQEVLDCDCDMASVHHLLSQIPQDLPYETLIS RXETFLFSFPHPNLLGRPLPNSKLRGRQPLLSKTLSWHQPSRGLIWCCGSGXR GLLRPEDRTKDVLTKPRTNRFVKLAVMGLTVALGAAALAVVKSALEWAPKF QLQLFP (SEQ ID NO:1162), AEVGTIFALSWLITWFGHVLSDFRHVVRLYD (SEQ ID NO:1163), and/or VLTKPRTNRFVKLAVMGLTVALGAAALAVVKSA (SEQ ID NO:1164). Moreover, fragments and variants of these polypeptides (such as, for example, fragments as described herein, polypeptides at least 80%, 85%, 90%, 95%, 96%, 97%, 98%, or 99% identical to these polypeptides and polypeptides encoded by the polynucleotide which hybridizes, under stringent conditions, to the polynucleotide encoding these polypeptides) are encompassed by the invention. Antibodies that bind polypeptides of the invention are also encompassed by the invention. Polynucleotides encoding these polypeptides are also encompassed by the invention.

The gene encoding the disclosed cDNA is believed to reside on chromosome 20. Accordingly, polynucleotides related to this invention are useful as a marker in linkage analysis for chromosome 20.

This gene is expressed primarily in osteoclastoma, microvascular endothelium, and bone marrow derived cell lines.

Polynucleotides and polypeptides of the invention are useful as reagents for differential identification of the tissue(s) or cell type(s) present in a biological sample and for diagnosis of diseases and conditions which include, but are not limited to, skeletal, vascular, or hematological diseases, particularly those involving aberrant

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proliferation of stem cells. Similarly, polypeptides and antibodies directed to these polypeptides are useful in providing immunological probes for differential identification of the tissue(s) or cell type(s). For a number of disorders of the above tissues or cells, particularly of the immune system, expression of this gene at significantly higher or lower levels may be routinely detected in certain tissues or cell types (e.g., skeletal, vascular, immune, hematological, and cancerous and wounded tissues) or bodily fluids (e.g., lymph, serum, plasma, urine, synovial fluid and spinal fluid) or another tissue or cell sample taken from an individual having such a disorder, relative to the standard gene expression level, i.e., the expression level in healthy tissue or bodily fluid from an individual not having the disorder.

Predicted epitopes include those comprising a sequence shown in SEQ ID NO: 430 as residues: Ser-33 to Ala-39.

The tissue distribution in bone marrow and endothelial cells indicates that the protein products of this gene is useful for treating disorders of the progenitors of the immune system. Applications include in vivo expansion of progenitor cells, ex vivo expansion of progenitor cells, or the treatment of tumors of the circulatory system, such as lymphomas. Moreover, the protein product of this gene may also show utility in either the enhancement or inhibition of immune cell localization or targeting at sites of inflammation or injury. The protein product of this gene may be useful in the treatment, detection, and/or prevention of a variety of vascular disorders, which include, but are not limited to microvascular disease, embolism, aneurysm, atherosclerosis, or stroke. Protein, as well as, antibodies directed against the protein may show utility as a tumor marker and/or immunotherapy targets for the above listed tissues.

Many polynucleotide sequences, such as EST sequences, are publicly available and accessible through sequence databases. Some of these sequences are related to SEQ ID NO:192 and may have been publicly available prior to conception of the present invention. Preferably, such related polynucleotides are specifically excluded from the scope of the present invention. To list every related sequence is cumbersome. Accordingly, preferably excluded from the present invention are one or more polynucleotides comprising a nucleotide sequence described by the general formula of a-b, where a is any integer between 1 to 2104 of SEQ ID NO:192, b is an

integer of 15 to 2118, where both a and b correspond to the positions of nucleotide residues shown in SEQ ID NO:192, and where b is greater than or equal to a + 14.

FEATURES OF PROTEIN ENCODED BY GENE NO: 183

In specific embodiments, polypeptides of the invention comprise, or alternatively consists of, an amino acid sequence selected from the group: GFGSVSAAGRRSGGTWQPVQ (SEQ ID NO:1165), PGGLAVG SRW WSRSLT (SEQ ID NO:1166), LEPSRQRRPRRRGGTSRPETDQRAKCWRQL (SEQ ID NO:1167), VCLRCQNRMEN (SEQ ID NO:1168), MAACTARRPGRGQPLVVPVADXGPVAKAALCAAXAGAFSPASTTTTRRHLS SRNRPEGKVLETVGVFEVPKQNGKYETGQLFLHSIFGYRGVVLFPWQARLXD RDVASAAPEKAENPAGHGSKEVKGKTHTYYQVLIDARDCPHISQRSQTEAVT FLANHDDSRALYAIPGLDYVSHEDILPYTSTDQVPIQHELFERFLLYDQTKAPP FVARETLRAWQEKNHPWLELSDVHRETTENIRVTVIPFYMGMREAQNSHVY WWRYCIRLENLDSDVVQLRERHWRIFSLSGTLETVRGRGVVGREPVLSKEQP AFQYSSHVSLQASSGHMWGTFRFERPDGSHFDVRIPPFSLESNKDEKTPPSGL HW (SEQ ID NO:1169), MAACTARRPGRGQPLVVPVADXGPVAKAALCAA (SEQ ID NO:1170), MAACTARRPGRGQPLVVPVADXGPVAKAALCAA (SEQ ID NO:1171), MAACTARRPGRGQPLVVPVADXGPVAKAALCAA (SEQ ID NO:1172), MAACTARRPGRGQPLVVPVADXGPVAKAALCAA (SEQ ID NO:1173), MAACTARRPGRGQPLVVPVADXGPVAKAALCAA (SEQ ID NO:1174), VLETVGVFEVPKQNGKYETGQLFLHSIFGYRGVVL (SEQ ID NO:1175), GLDYVSHEDILPYTST (SEQ ID NO:1176), DVHRETTENIRVTVIPFYM (SEQ ID NO:1177), WWRYCIRLENLDSDVVQLRER (SEQ ID NO:1178), PAFQYSSHVSLQASSGHMWGTFRFER (SEQ ID NO:1179), RLPSHKRRCFCLVIQKKSFKEFMLDGNLISGGVGEDVFMADIVQAWDGIEGP TVIMVSQEGHSFCLRSLRYMWAVTSINQHLIVSVSFAFHLLGAMASRVLCFF WSCRSHIPVXQSGLPGKQDDTSVAKNAMKEKLPGLIFSILFWHLKHTNCLQH FALWSVSGREVPPRRRGRRWREGSSXGRAQSGLGHRAXVSDRDHQRLPTAR

PPGCTGCHVPPERRPAADTEPNP (SEQ ID NO:1180), KEFMLDGNLISGGVGEDVFMADIVQAWDGIE (SEQ ID NO:1181), AVTSINQHLIVSVSFAFHLLGAMASRVLC (SEQ ID NO:1182), and/or TARPPGCTGCHVPPERRPAA (SEQ ID NO:1183). Moreover, fragments and variants of these polypeptides (such as, for example, fragments as described herein, polypeptides at least 80%, 85%, 90%, 95%, 96%, 97%, 98%, or 99% identical to these polypeptides and polypeptides encoded by the polynucleotide which hybridizes, under stringent conditions, to the polynucleotide encoding these polypeptides) are encompassed by the invention. Antibodies that bind polypeptides of the invention are also encompassed by the invention. Polynucleotides encoding these polypeptides are also encompassed by the invention.

The gene encoding the disclosed cDNA is believed to reside on chromosome 17. Accordingly, polynucleotides related to this invention are useful as a marker in linkage analysis for chromosome 17.

This gene is expressed primarily in gall bladder, prostate, and fetal brain, and to a lesser extent, in tumor and fetal tissues.

Polynucleotides and polypeptides of the invention are useful as reagents for differential identification of the tissue(s) or cell type(s) present in a biological sample and for diagnosis of diseases and conditions which include, but are not limited to, gastrointestinal, reproductive, neural, or growth related disorders such as cancers. Similarly, polypeptides and antibodies directed to these polypeptides are useful in providing immunological probes for differential identification of the tissue(s) or cell type(s). For a number of disorders of the above tissues or cells, particularly of the prostate, gall bladder, and fetal brain, expression of this gene at significantly higher or lower levels may be routinely detected in certain tissues or cell types (e.g., gastrointestinal, reproductive, neural, developmental, and cancerous and wounded tissues) or bodily fluids (e.g., lymph, amniotic fluid, bile, serum, plasma, urine, synovial fluid and spinal fluid) or another tissue or cell sample taken from an individual having such a disorder, relative to the standard gene expression level, i.e., the expression level in healthy tissue or bodily fluid from an individual not having the disorder.

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The tissue distribution in fetal brain and tumor tissues indicates that the protein product of this gene is useful for the diagnosis and treatment of growth-related disorders, such as cancers. Moreover, the protein product of this gene is useful for the detection/treatment of neurodegenerative disease states, behavioral disorders, or inflammatory conditions which include, but are not limited to Alzheimer's Disease, Parkinson's Disease, Huntington's Disease, Tourette's Syndrome, meningitis, encephalitis, demyelinating diseases, peripheral neuropathies, neoplasia, trauma, congenital malformations, spinal cord injuries, ischemia and infarction, aneurysms, hemorrhages, schizophrenia, mania, dementia, paranoia, obsessive compulsive disorder, depression, panic disorder, learning disabilities, ALS, psychoses, autism, and altered behaviors, including disorders in feeding, sleep patterns, balance, and perception. In addition, elevated expression of this gene product in regions of the brain indicates that it plays a role in normal neural function. Potentially, this gene product is involved in synapse formation, neurotransmission, learning, cognition, homeostasis, or neuronal differentiation or survival, in addition to metabolic, or reproductive disorders. Protein, as well as, antibodies directed against the protein may show utility as a tumor marker and/or immunotherapy targets for the above listed tissues.

Many polynucleotide sequences, such as EST sequences, are publicly available and accessible through sequence databases. Some of these sequences are related to SEQ ID NO:193 and may have been publicly available prior to conception of the present invention. Preferably, such related polynucleotides are specifically excluded from the scope of the present invention. To list every related sequence is cumbersome. Accordingly, preferably excluded from the present invention are one or more polynucleotides comprising a nucleotide sequence described by the general formula of a-b, where a is any integer between 1 to 1524 of SEQ ID NO:193, b is an integer of 15 to 1538, where both a and b correspond to the positions of nucleotide residues shown in SEQ ID NO:193, and where b is greater than or equal to a + 14.

FEATURES OF PROTEIN ENCODED BY GENE NO: 184

In specific embodiments, polypeptides of the invention comprise, or alternatively consists of, an amino acid sequence selected from the group: SLCCPEGAEGC (SEQ ID NO:1184), QLKKTHYDRPCP (SEQ ID NO:1185), QLKKTHYDRPCP (SEQ ID NO:1186), MNRPCPFCLWKVFPLLLLLHEELFPLPVP (SEQ ID NO:1187), and/or KEKTFTPRNSLCCPEGAEGCIAGGDLQLKKTHY (SEQ ID NO:1188). Moreover, fragments and variants of these polypeptides (such as, for example, fragments as described herein, polypeptides at least 80%, 85%, 90%, 95%, 96%, 97%, 98%, or 99% identical to these polypeptides and polypeptides encoded by the polynucleotide which hybridizes, under stringent conditions, to the polynucleotide encoding these polypeptides) are encompassed by the invention. Antibodies that bind polypeptides of the invention are also encompassed by the invention. Polynucleotides encoding these polypeptides are also encompassed by the invention.

This gene is expressed primarily in stromal cell, tonsil, and glioblastoma.

Polynucleotides and polypeptides of the invention are useful as reagents for differential identification of the tissue(s) or cell type(s) present in a biological sample and for diagnosis of diseases and conditions which include, but are not limited to, hematopoietic, immune and inflammatory disorders, in addition to neural disorders, such as glioblastoma. Similarly, polypeptides and antibodies directed to these polypeptides are useful in providing immunological probes for differential identification of the tissue(s) or cell type(s). For a number of disorders of the above tissues or cells, particularly of the stromal cells, tonsil, and glioblastoma expression of this gene at significantly higher or lower levels may be routinely detected in certain tissues or cell types (e.g., immune, hematopoietic, neural, and cancerous and wounded tissues) or bodily fluids (e.g., lymph, serum, plasma, urine, synovial fluid and spinal fluid) or another tissue or cell sample taken from an individual having such a disorder, relative to the standard gene expression level, i.e., the expression level in healthy tissue or bodily fluid from an individual not having the disorder.

Additionally, it is believed that the product of this gene regulates pancreatic cell differentiation into beta cells. Accordingly, polynucleotides and polypeptides of the invention are useful in the treatment of insulin-dependent diabetes mellitus and

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associated conditions e.g. pancreatic hypofunction and the prevention, as well as the treatment of undifferentiated type pancreatic cancers.

Predicted epitopes include those comprising a sequence shown in SEQ ID NO: 432 as residues: Pro-27 to Ala-32.

The tissue distribution in stromal cells and tonsils indicates that the protein product of this gene is useful for diagnosis and treatment of immune and inflammatory disorders and glioblastoma. Similarly, the protein product of this gene is useful for the treatment and diagnosis of hematopoetic related disorders such as anemia, pancytopenia, leukopenia, thrombocytopenia or leukemia since stromal cells are important in the production of cells of hematopoietic lineages. The uses include bone marrow cell ex vivo culture, bone marrow transplantation, bone marrow reconstitution, radiotherapy or chemotherapy of neoplasia. The gene product may also be involved in lymphopoiesis, therefore, it can be used in immune disorders such as infection, inflammation, allergy, immunodeficiency etc. In addition, this gene product may have commercial utility in the expansion of stem cells and committed progenitors of various blood lineages, and in the differentiation and/or proliferation of various cell types. Protein, as well as, antibodies directed against the protein may show utility as a tumor marker and/or immunotherapy targets for the above listed tissues.

Many polynucleotide sequences, such as EST sequences, are publicly available and accessible through sequence databases. Some of these sequences are related to SEQ ID NO:194 and may have been publicly available prior to conception of the present invention. Preferably, such related polynucleotides are specifically excluded from the scope of the present invention. To list every related sequence is cumbersome. Accordingly, preferably excluded from the present invention are one or more polynucleotides comprising a nucleotide sequence described by the general formula of a-b, where a is any integer between 1 to 1084 of SEQ ID NO:194, b is an integer of 15 to 1098, where both a and b correspond to the positions of nucleotide residues shown in SEQ ID NO:194, and where b is greater than or equal to a + 14.

FEATURES OF PROTEIN ENCODED BY GENE NO: 185

This gene is expressed primarily in hepatocellular carcinoma.

Polynucleotides and polypeptides of the invention are useful as reagents for differential identification of the tissue(s) or cell type(s) present in a biological sample and for diagnosis of diseases and conditions which include, but are not limited to, hepatic or metabolic diseases. Similarly, polypeptides and antibodies directed to these polypeptides are useful in providing immunological probes for differential identification of the tissue(s) or cell type(s). For a number of disorders of the above tissues or cells, particularly of the liver, expression of this gene at significantly higher or lower levels may be routinely detected in certain tissues or cell types (e.g., hepatic, metabolic, immune, hematopoietic, and cancerous and wounded tissues) or bodily fluids (e.g., lymph, serum, bile, plasma, urine, synovial fluid and spinal fluid) or another tissue or cell sample taken from an individual having such a disorder, relative to the standard gene expression level, i.e., the expression level in healthy tissue or bodily fluid from an individual not having the disorder.

Predicted epitopes include those comprising a sequence shown in SEQ ID NO: 433 as residues: Gly-32 to Lys-39.

The tissue distribution in hepatocellular carcinoma tissue indicates that the protein product of this gene is useful for diagnosis and treatment of liver diseases. Moreover, the protein product of this gene is useful for the detection and treatment of liver disorders and cancers (e.g. hepatoblastoma, jaundice, hepatitis, liver metabolic diseases and conditions that are attributable to the differentiation of hepatocyte progenitor cells). In addition the protein may have a useful role in treating, detecting, or preventing developmental abnormalities, fetal deficiencies, pre-natal disorders and various would-healing models and/or tissue trauma. Protein, as well as, antibodies directed against the protein may show utility as a tumor marker and/or immunotherapy targets for the above listed tissues.

Many polynucleotide sequences, such as EST sequences, are publicly available and accessible through sequence databases. Some of these sequences are related to SEQ ID NO:195 and may have been publicly available prior to conception of the present invention. Preferably, such related polynucleotides are specifically excluded from the scope of the present invention. To list every related sequence is

cumbersome. Accordingly, preferably excluded from the present invention are one or more polynucleotides comprising a nucleotide sequence described by the general formula of a-b, where a is any integer between 1 to 987 of SEQ ID NO:195, b is an integer of 15 to 1001, where both a and b correspond to the positions of nucleotide residues shown in SEQ ID NO:195, and where b is greater than or equal to a + 14.

FEATURES OF PROTEIN ENCODED BY GENE NO: 186

This gene is expressed primarily in hippocampus.

Polynucleotides and polypeptides of the invention are useful as reagents for differential identification of the tissue(s) or cell type(s) present in a biological sample and for diagnosis of diseases and conditions which include, but are not limited to, neuronal or endocrine disorders, particularly behavioral and mood disorders. Similarly, polypeptides and antibodies directed to these polypeptides are useful in providing immunological probes for differential identification of the tissue(s) or cell type(s). For a number of disorders of the above tissues or cells, particularly of the hippocampus, expression of this gene at significantly higher or lower levels may be routinely detected in certain tissues or cell types (e.g., neural, endocrine, and cancerous and wounded tissues) or bodily fluids (e.g., lymph, serum, plasma, urine, synovial fluid and spinal fluid) or another tissue or cell sample taken from an individual having such a disorder, relative to the standard gene expression level, i.e., the expression level in healthy tissue or bodily fluid from an individual not having the disorder.

Predicted epitopes include those comprising a sequence shown in SEQ ID NO: 434 as residues: Ser-14 to Tyr-20.

The tissue distribution in hippocampus indicates that the protein product of this gene is useful for the diagnosis and treatment of neuronal disorders. Moreover, the protein product of this gene is useful for the detection/treatment of neurodegenerative disease states, behavioral disorders, or inflammatory conditions which include, but are not limited to Alzheimer's Disease, Parkinson's Disease, Huntington's Disease, Tourette's Syndrome, meningitis, encephalitis, demyelinating

diseases, peripheral neuropathies, neoplasia, trauma, congenital malformations, spinal cord injuries, ischemia and infarction, aneurysms, hemorrhages, schizophrenia, mania, dementia, paranoia, obsessive compulsive disorder, depression, panic disorder, learning disabilities, ALS, psychoses, autism, and altered behaviors, including disorders in feeding, sleep patterns, balance, and perception. In addition, elevated expression of this gene product in regions of the brain indicates that it plays a role in normal neural function. Potentially, this gene product is involved in synapse formation, neurotransmission, learning, cognition, homeostasis, or neuronal differentiation or survival. Protein, as well as, antibodies directed against the protein may show utility as a tumor marker and/or immunotherapy targets for the above listed tissues.

Many polynucleotide sequences, such as EST sequences, are publicly available and accessible through sequence databases. Some of these sequences are related to SEQ ID NO:196 and may have been publicly available prior to conception of the present invention. Preferably, such related polynucleotides are specifically excluded from the scope of the present invention. To list every related sequence is cumbersome. Accordingly, preferably excluded from the present invention are one or more polynucleotides comprising a nucleotide sequence described by the general formula of a-b, where a is any integer between 1 to 1444 of SEQ ID NO:196, b is an integer of 15 to 1458, where both a and b correspond to the positions of nucleotide residues shown in SEQ ID NO:196, and where b is greater than or equal to a + 14.

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FEATURES OF PROTEIN ENCODED BY GENE NO: 187

This gene is expressed primarily in bone cancer and hippocampus, and to a lesser extent, in osteoclastoma.

Polynucleotides and polypeptides of the invention are useful as reagents for differential identification of the tissue(s) or cell type(s) present in a biological sample and for diagnosis of diseases and conditions which include, but are not limited to, bone-related disorders and neuronal diseases. Similarly, polypeptides and antibodies directed to these polypeptides are useful in providing immunological probes for

differential identification of the tissue(s) or cell type(s). For a number of disorders of the above tissues or cells, particularly of the bone, osteoclast, and hippocampus, expression of this gene at significantly higher or lower levels may be routinely detected in certain tissues or cell types (e.g., neural, skeletal, and cancerous and wounded tissues) or bodily fluids (e.g., lymph, serum, plasma, urine, synovial fluid and spinal fluid) or another tissue or cell sample taken from an individual having such a disorder, relative to the standard gene expression level, i.e., the expression level in healthy tissue or bodily fluid from an individual not having the disorder.

The tissue distribution in hippocampus and skeletal tissues indicates that the protein product of this gene is useful for diagnosis and treatment of bone-related disorders and neuronal diseases. Similarly, this gene product is useful in the detection and treatment of disorders and conditions affecting the skeletal system, in particular osteoporosis, bone cancer, as well as, disorders afflicting connective tissues (e.g. arthritis, trauma, tendonitis, chrondomalacia and inflammation), such as in the diagnosis or treatment of various autoimmune disorders such as rheumatoid arthritis, lupus, scleroderma, and dermatomyositis as well as dwarfism, spinal deformation, and specific joint abnormalities as well as chondrodysplasias (i.e. spondyloepiphyseal dysplasia congenita, familial osteoarthritis, Atelosteogenesis type II, metaphyseal chondrodysplasia type Schmid). Alternatively, the protein product of this gene is useful for the detection/treatment of neurodegenerative disease states, behavioral disorders, or inflammatory conditions. Protein, as well as, antibodies directed against the protein may show utility as a tumor marker and/or immunotherapy targets for the above listed tissues.

Many polynucleotide sequences, such as EST sequences, are publicly available and accessible through sequence databases. Some of these sequences are related to SEQ ID NO:197 and may have been publicly available prior to conception of the present invention. Preferably, such related polynucleotides are specifically excluded from the scope of the present invention. To list every related sequence is cumbersome. Accordingly, preferably excluded from the present invention are one or more polynucleotides comprising a nucleotide sequence described by the general formula of a-b, where a is any integer between 1 to 1268 of SEQ ID NO:197, b is an

integer of 15 to 1282, where both a and b correspond to the positions of nucleotide residues shown in SEQ ID NO:197, and where b is greater than or equal to a + 14.

FEATURES OF PROTEIN ENCODED BY GENE NO: 188

The gene encoding the disclosed cDNA is thought to reside on chromosome 4. Accordingly, polynucleotides related to this invention are useful as a marker in linkage analysis for chromosome 4.

This gene is expressed primarily in neuronal tissues such as hippocampus, spinal cord, and hypothalamus.

Polynucleotides and polypeptides of the invention are useful as reagents for differential identification of the tissue(s) or cell type(s) present in a biological sample and for diagnosis of diseases and conditions which include, but are not limited to, neuronal diseases. Similarly, polypeptides and antibodies directed to these polypeptides are useful in providing immunological probes for differential identification of the tissue(s) or cell type(s). For a number of disorders of the above tissues or cells, particularly of the neuronal tissues, expression of this gene at significantly higher or lower levels may be routinely detected in certain tissues or cell types (e.g. neuronal, cancerous and wounded tissues) or bodily fluids (e.g., lymph, serum, plasma, urine, synovial fluid and spinal fluid) or another tissue or cell sample taken from an individual having such a disorder, relative to the standard gene expression level, i.e., the expression level in healthy tissue or bodily fluid from an individual not having the disorder.

The tissue distribution in neuronal tissues indicates that the protein product of this gene is useful for diagnosis and treatment of neuronal disorders, such as Alzheimer's Disease, Parkinson's Disease, Huntington's Disease, Tourette's Syndrome, schizophrenia, mania, dementia, paranoia, obsessive compulsive disorder, panic disorder, learning disabilities, ALS, psychoses, autism, and altered behaviors, including disorders in feeding, sleep patterns, balance, and perception. In addition, the gene or gene product may also play a role in the treatment and/or detection of developmental disorders associated with the developing embryo, or sexually-linked

disorders. Protein, as well as, antibodies directed against the protein may show utility as a tumor marker and/or immunotherapy targets for the above listed tissues.

Many polynucleotide sequences, such as EST sequences, are publicly available and accessible through sequence databases. Some of these sequences are related to SEQ ID NO:198 and may have been publicly available prior to conception of the present invention. Preferably, such related polynucleotides are specifically excluded from the scope of the present invention. To list every related sequence is cumbersome. Accordingly, preferably excluded from the present invention are one or more polynucleotides comprising a nucleotide sequence described by the general formula of a-b, where a is any integer between 1 to 937 of SEQ ID NO:198, b is an integer of 15 to 951, where both a and b correspond to the positions of nucleotide residues shown in SEQ ID NO:198, and where b is greater than or equal to a + 14.

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FEATURES OF PROTEIN ENCODED BY GENE NO: 189

The gene encoding the disclosed cDNA is thought to reside on chromosome 10. Accordingly, polynucleotides related to this invention are useful as a marker in linkage analysis for chromosome 10.

This gene is expressed primarily in neuronal tissues and immune tissues.

Polynucleotides and polypeptides of the invention are useful as reagents for differential identification of the tissue(s) or cell type(s) present in a biological sample and for diagnosis of diseases and conditions which include, but are not limited to, neuronal and immune-related disorders. Similarly, polypeptides and antibodies directed to these polypeptides are useful in providing immunological probes for differential identification of the tissue(s) or cell type(s). For a number of disorders of the above tissues or cells, particularly of the neuronal and immune-related tissues, expression of this gene at significantly higher or lower levels may be routinely detected in certain tissues or cell types (e.g. neuronal, immune, cancerous and wounded tissues) or bodily fluids (e.g., lymph, serum, plasma, urine, synovial fluid and spinal fluid) or another tissue or cell sample taken from an individual having such

a disorder, relative to the standard gene expression level, i.e., the expression level in healthy tissue or bodily fluid from an individual not having the disorder.

Predicted epitopes include those comprising a sequence shown in SEQ ID NO: 437 as residues: Pro-19 to Asp-25.

The tissue distribution neuronal and immune tissues indicates that the protein product of this gene is useful for the diagnosis and treatment of neuronal and immune-related disorders. Furthermore, the tissue distribution indicates that the protein product of this gene is useful for the detection/treatment of neurodegenerative disease states, neuronal disorders, and behavioral disorders such as Alzheimer's Disease, Parkinson's Disease, Huntington's Disease, Tourette's Syndrome, schizophrenia, mania, dementia, paranoia, obsessive compulsive disorder, panic disorder, learning disabilities, ALS, psychoses, autism, and altered behaviors, including disorders in feeding, sleep patterns, balance, and perception. In addition, the gene or gene product may also play a role in the treatment and/or detection of developmental disorders associated with the developing embryo, or sexually-linked disorders. Additionally, this gene product may be involved in the regulation of cytokine production, antigen presentation, or other processes that may also suggest a usefulness in the treatment of cancer (e.g. by boosting immune responses). Since the gene is expressed in cells of lymphoid origin, the gene or protein, as well as, antibodies directed against the protein may show utility as a tumor marker and/or immunotherapy targets for the above listed tissues. Therefore it may be also used as an agent for immunological disorders including arthritis, asthma, immune deficiency diseases such as AIDS, leukemia, rheumatoid arthritis, inflammatory bowel disease, sepsis, acne, and psoriasis. In addition, this gene product may have commercial utility in the expansion of stem cells and committed progenitors of various blood lineages, and in the differentiation and/or proliferation of various cell types. Protein, as well as, antibodies directed against the protein may show utility as a tumor marker and/or immunotherapy targets for the above listed tissues.

Many polynucleotide sequences, such as EST sequences, are publicly available and accessible through sequence databases. Some of these sequences are related to SEQ ID NO:199 and may have been publicly available prior to conception of the present invention. Preferably, such related polynucleotides are specifically

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excluded from the scope of the present invention. To list every related sequence is cumbersome. Accordingly, preferably excluded from the present invention are one or more polynucleotides comprising a nucleotide sequence described by the general formula of a-b, where a is any integer between 1 to 1726 of SEQ ID NO:199, b is an integer of 15 to 1740, where both a and b correspond to the positions of nucleotide residues shown in SEQ ID NO:199, and where b is greater than or equal to a + 14.

FEATURES OF PROTEIN ENCODED BY GENE NO: 190

The translation product of this gene shares sequence homology with human N33, a gene located in a homozygously deleted region of human metastatic prostate cancer, which is thought to be important in prevention of prostate cancer. The gene and its translation product also share sequence homology with an isolated prostate/colon tumor suppressor gene (PSTG) product (WO9532214-A1.).

In specific embodiments, polypeptides of the invention comprise, or alternatively consists of, an amino acid sequence selected from the group: AQRKKEMVLSEKVSQLMEWTNKRPVIRMNGDKFRRLVKAPPRNYSVIVMFT ALQLHRQCVVCKQADEEFQILANSWRYSSAFTNRIFFAMVDFDEGSDVFQML NMNSAPTFINFPAKGKPKRGDTYELQVRGFSAEQIARWIADRTDVNIRVIRPP NMAARWRFWCVSVT (SEQ ID NO:1189), MVVALLIVCDVPSAS (SEQ ID NO:1190), AQRKKEMVLSEKVSQL (SEQ ID NO:1191), MEWTNKRPVIRMNGDKF (SEQ ID:1192), RRLVKAPPRNYSVIVMFTALQLHRQCVVCKQADEEFQILANSWRYSSAFTNR IFFA (SEQ ID NO:1193), MVDFDEGSDVFQMLNMNSAPTFINFPAKGKP (SEQ ID NO:1194), KRGDTYELQVRGFSAEQIARWIADRTDVNIRVIRPPN (SEQ ID NO:1195), and/or YAGPLMLGLLLAVIGGLVYLRRVIWNFSLIKLDGLLQLCVLCLL (SEQ ID NO:1196). Moreover, fragments and variants of these polypeptides (such as, for example, fragments as described herein, polypeptides at least 80%, 85%, 90%, 95%, 96%, 97%, 98%, or 99% identical to these polypeptides and polypeptides encoded by the polynucleotide which hybridizes, under stringent conditions, to the polynucleotide

encoding these polypeptides) are encompassed by the invention. Antibodies that bind polypeptides of the invention are also encompassed by the invention. Polynucleotides encoding these polypeptides are also encompassed by the invention.

This gene is expressed primarily in infant adrenal gland, prostate cell line, and to a lesser extent in adrenal gland.

Polynucleotides and polypeptides of the invention are useful as reagents for differential identification of the tissue(s) or cell type(s) present in a biological sample and for diagnosis of diseases and conditions which include, but are not limited to, prostate cancer and endocrine disorders. Similarly, polypeptides and antibodies directed to these polypeptides are useful in providing immunological probes for differential identification of the tissue(s) or cell type(s). For a number of disorders of the above tissues or cells, particularly of the prostate and adrenal gland, expression of this gene at significantly higher or lower levels may be routinely detected in certain tissues or cell types (e.g. prostate, endocrine, cancerous and wounded tissues) or bodily fluids (e.g., lymph, serum, plasma, urine, synovial fluid and spinal fluid) or another tissue or cell sample taken from an individual having such a disorder, relative to the standard gene expression level, i.e., the expression level in healthy tissue or bodily fluid from an individual not having the disorder.

Predicted epitopes include those comprising a sequence shown in SEQ ID NO: 438 as residues: Pro-34 to Gly-43, Arg-113 to Pro-120.

The tissue distribution infant adrenal gland, combined with the homology to N33 and prostate/colon tumor suppressor gene (PSTG) indicates that the protein product of this gene is useful for the diagnosis and treatment for prostate cancer and endocrine disorders, and that the nucleic acids and proteins of this gene can be used in the diagnosis and treatment of prostate, endocrine and colorectal cancers. Protein, as well as, antibodies directed against the protein may show utility as a tumor marker and immunotherapy targets for the above listed tumors and tissues.

Many polynucleotide sequences, such as EST sequences, are publicly available and accessible through sequence databases. Some of these sequences are related to SEQ ID NO:200 and may have been publicly available prior to conception of the present invention. Preferably, such related polynucleotides are specifically excluded from the scope of the present invention. To list every related sequence is

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cumbersome. Accordingly, preferably excluded from the present invention are one or more polynucleotides comprising a nucleotide sequence described by the general formula of a-b, where a is any integer between 1 to 1693 of SEQ ID NO:200, b is an integer of 15 to 1707, where both a and b correspond to the positions of nucleotide residues shown in SEQ ID NO:200, and where b is greater than or equal to a + 14.

FEATURES OF PROTEIN ENCODED BY GENE NO: 191

This gene is expressed primarily in T-cell, and to a lesser extent in fetal lung.

Polynucleotides and polypeptides of the invention are useful as reagents for differential identification of the tissue(s) or cell type(s) present in a biological sample and for diagnosis of diseases and conditions which include, but are not limited to, immune and respiratory disorders. Similarly, polypeptides and antibodies directed to these polypeptides are useful in providing immunological probes for differential identification of the tissue(s) or cell type(s). For a number of disorders of the above tissues or cells, particularly of the immune and respiratory systems, expression of this gene at significantly higher or lower levels may be routinely detected in certain tissues or cell types (e.g. immune, respiratory, cancerous and wounded tissues) or bodily fluids (e.g., lymph, serum, plasma, urine, synovial fluid and spinal fluid) or another tissue or cell sample taken from an individual having such a disorder, relative to the standard gene expression level, i.e., the expression level in healthy tissue or bodily fluid from an individual not having the disorder.

Predicted epitopes include those comprising a sequence shown in SEQ ID NO: 439 as residues: Trp-3 to Phe-9.

The tissue distribution in T-cells and fetal lung indicates that the protein product of this gene is useful for the diagnosis and treatment of immune and respiratory disorders. Furthermore, this gene product may be involved in the regulation of cytokine production, antigen presentation, or other processes that may also suggest a usefulness in the treatment of cancer (e.g. by boosting immune responses). Since the gene is expressed in cells of lymphoid origin, the gene or protein, as well as, antibodies directed against the protein may show utility as a tumor

marker and/or immunotherapy targets for the above listed tissues. Therefore it may be also used as an agent for immunological disorders including arthritis, asthma, immune deficiency diseases such as AIDS, leukemia, rheumatoid arthritis, inflammatory bowel disease, sepsis, acne, and psoriasis. In addition, this gene product may have commercial utility in the expansion of stem cells and committed progenitors of various blood lineages, and in the differentiation and/or proliferation of various cell types. Expression of this gene product in T cells also strongly indicates a role for this protein in immune function and immune surveillance. The tissue distribution also indicates that the protein product of this gene is useful for the detection and treatment of disorders associated with developing lungs, particularly in premature infants where the lungs are the last tissues to develop. The tissue distribution indicates that the protein product of this gene is useful for the diagnosis and intervention of lung tumors, since the gene may be involved in the regulation of cell division, particularly since it is expressed in fetal tissue. Protein, as well as, antibodies directed against the protein may show utility as a tumor marker and/or immunotherapy targets for the above listed tissues.

Many polynucleotide sequences, such as EST sequences, are publicly available and accessible through sequence databases. Some of these sequences are related to SEQ ID NO:201 and may have been publicly available prior to conception of the present invention. Preferably, such related polynucleotides are specifically excluded from the scope of the present invention. To list every related sequence is cumbersome. Accordingly, preferably excluded from the present invention are one or more polynucleotides comprising a nucleotide sequence described by the general formula of a-b, where a is any integer between 1 to 765 of SEQ ID NO:201, b is an integer of 15 to 779, where both a and b correspond to the positions of nucleotide residues shown in SEQ ID NO:201, and where b is greater than or equal to a + 14.

FEATURES OF PROTEIN ENCODED BY GENE NO: 192

The gene encoding the disclosed cDNA is thought to reside on chromosome 6. Accordingly, polynucleotides related to this invention are useful as a marker in

linkage analysis for chromosome 6. The translation product of this gene shares significant homology with the rat protein Neuritin, and in fact appears to be a human ortholog of the rat protein. It is believed that this gene is induced in rats by neural activity and neurotrophins, and that it promotes neuritogenesis. Neural activity and neurotrophins induce synaptic remodeling in part by altering gene expression. This gene is believed to be a glycosylphoshatidylinositol-anchored protein encoded by a hippocampal gene, and to possess neural activity. This molecule is believed to be expressed in post-mitotic differentiating neurons of the developing nervous system and neuronal structures associated with plasticity in the adult. Message of this gene is believed to be induced by neuronal activity and by the activity-regulated neurotrophins BDNF and NT-3. The product of this gene is believed to stimulate neurite outgrowth and arborization in primary embryonic hippocampal and cortical cultures, and to act as a downstream effector of activity-induced neurite outgrowth.

In specific embodiments, polypeptides of the invention comprise, or alternatively consists of, an amino acid sequence selected from the group: DAVFKGFSDCLLKLGDS (SEQ ID NO:1197), CQEGAKDMWDKLRKESKNLN (SEQ ID NO:1198), VLLVSLSAALATWLSF (SEQ ID NO:1199), MGLKLNGRYISLILAVQIAYLVQAVRAAGKCDAVFKGFSDCLLKLGDS (SEQ ID NO:1200), PAAWDDKTNIKTVCTYWEDFHSCTVTALTDCQEGAKDMWDKLRKESKNLN IQGSLFELCGSGNGAAGSLLPAFPVLLVSLSAALATWLSF (SEQ ID NO:1201), and/or

MGLKLNGRYISLILAVQIAYLVQAVRAAGKCDAVFKGFSDCLLKLGDSXXX XXPAAWDDKTNIKTVCTYWEDFHSCTVTALTDCQEGAKDMWDKLRKESKN LNIQGSLFELCGSGNGAAGSLLPAFPVLLVSLSAALATWLSF (SEQ ID NO:1202). Moreover, fragments and variants of these polypeptides (such as, for example, fragments as described herein, polypeptides at least 80%, 85%, 90%, 95%, 96%, 97%, 98%, or 99% identical to these polypeptides and polypeptides encoded by the polynucleotide which hybridizes, under stringent conditions, to the polynucleotide encoding these polypeptides) are encompassed by the invention. Antibodies that bind polypeptides of the invention are also encompassed by the invention. Polynucleotides encoding these polypeptides are also encompassed by the invention.

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This gene is expressed primarily in human placenta, endometrial tumor and tissues of the central nervous system (CNS).

Polynucleotides and polypeptides of the invention are useful as reagents for differential identification of the tissue(s) or cell type(s) present in a biological sample and for diagnosis of diseases and conditions which include, but are not limited to, relating to reproductive disorders, cancers and neurological diseases. Similarly, polypeptides and antibodies directed to these polypeptides are useful in providing immunological probes for differential identification of the tissue(s) or cell type(s). For a number of disorders of the above tissues or cells, particularly of the reproductive and neurological disorders, expression of this gene at significantly higher or lower levels may be routinely detected in certain tissues or cell types (e.g. reproductive, neurological, cancerous and wounded tissues) or bodily fluids (e.g., lymph, serum, plasma, urine, synovial fluid and spinal fluid) or another tissue or cell sample taken from an individual having such a disorder, relative to the standard gene expression level, i.e., the expression level in healthy tissue or bodily fluid from an individual not having the disorder.

Predicted epitopes include those comprising a sequence shown in SEQ ID NO: 440 as residues: Asp-47 to Asp-63, His-75 to Tyr-80, Pro-83 to Tyr-89.

The tissue distribution indicates that the protein product of this gene is useful for the diagnosis and treatment of reproductive disorders such as endometrial tumors. Expression of this gene in tissues of the CNS, and its strong homology to Neuritin, suggest that the protein product from this gene is also useful in the treatment and diagnosis of neurological disorders and in the regeneration of neural tissues, e.g., following injury.

Many polynucleotide sequences, such as EST sequences, are publicly available and accessible through sequence databases. Some of these sequences are related to SEQ ID NO:202 and may have been publicly available prior to conception of the present invention. Preferably, such related polynucleotides are specifically excluded from the scope of the present invention. To list every related sequence is cumbersome. Accordingly, preferably excluded from the present invention are one or more polynucleotides comprising a nucleotide sequence described by the general formula of a-b, where a is any integer between 1 to 1603 of SEQ ID NO:202, b is an

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integer of 15 to 1617, where both a and b correspond to the positions of nucleotide residues shown in SEQ ID NO:202, and where b is greater than or equal to a + 14.

FEATURES OF PROTEIN ENCODED BY GENE NO: 193

The translation product of this gene shares sequence homology with tenascin, which is thought to be important in development. The translation product of this gene is believed to be a ligand of the fibroblast growth factor family. FGF ligand activity is known in the art and can be assayed by methods known in the art and disclosed elsewhere herein.

Northern analysis indicates that a 2.5 kb band is expressed in brain and lung. It has also been discovered that this gene is expressed in endometrial tumor, synovial sarcoma, pancreas tumor, fetal lung, retinal, and immune tissues (e.g., bone marrow)

Polynucleotides and polypeptides of the invention are useful as reagents for differential identification of the tissue(s) or cell type(s) present in a biological sample and for diagnosis of diseases and conditions which include, but are not limited to, cancers, growth disorders of the brain and lung. Similarly, polypeptides and antibodies directed to these polypeptides are useful in providing immunological probes for differential identification of the tissue(s) or cell type(s). For a number of disorders of the above tissues or cells, particularly of the cancer tissues, brain, lung, expression of this gene at significantly higher or lower levels may be routinely detected in certain tissues or cell types (e.g. brain, lung, cancerous and wounded tissues) or bodily fluids (e.g., lymph, serum, plasma, urine, synovial fluid and spinal fluid) or another tissue or cell sample taken from an individual having such a disorder, relative to the standard gene expression level, i.e., the expression level in healthy tissue or bodily fluid from an individual not having the disorder.

Predicted epitopes include those comprising a sequence shown in SEQ ID NO: 441 as residues: Gly-29 to Glu-34, Arg-71 to Arg-76, Thr-176 to Cys-182, Gly-184 to Glu-199. As a preferred embodiment, antibodies that bind said epitopes are encompassed by the invention and may be useful as a cancer diagnostic and/or an agonist/antagonist of the polypeptides of the invention.

Fragments and variants of the polypeptide encoded by this gene (such as, for example, fragments as described herein, polypeptides at least 80%, 85%, 90%, 95%, 96%, 97%, 98%, or 99% identical to these polypeptides and polypeptides encoded by the polynucleotide which hybridizes, under stringent conditions, to the polynucleotide encoding these polypeptides , or the complement there of are encompassed by the invention). Antibodies that bind polypeptides of the invention are also encompassed by the invention. Polynucleotides encoding these polypeptides are also encompassed by the invention. Antibodies that bind polypeptides of the invention would be useful as a cancer diagnostic.

Preferred polypeptide fragments of the invention comprise, or alternatively consist of, the secreted protein having a continuous series of deleted residues from the amino or the carboxy terminus, or both. Particularly, N-terminal deletions of the polypeptide can be described by the general formula m-379 where m is an integer from 2 to 371, where m corresponds to the position of the amino acid residue identified in SEQ ID NO:441. More in particular, the invention provides polynucleotides encoding polypeptides comprising, or alternatively consisting of, an amino acid sequence selected from the group: A-2 to W-379; R-3 toW-379; R-4 to W-379; S-5 to W-379; A-6 to W-379; F-7 toW-379; P-8 to W-379; A-9 to W-379; A-10 to W-379; A-11to W-379; L-12 to W-379; W-13 to W-379; L-14 to W-379;W-15 to W-379; S-16 to W-379; I-17 to W-379; L-18 toW-379; L-19 to W-379; C-20 to W-379; L-21 to W-379; L-22to W-379; A-23 to W-379; L-24 to W-379; R-25 to W-379;A-26 to W-379; E-27 to W-379; A-28 to W-379; G-29 toW-379; P-30 to W-379; P-31 to W-379; Q-32 to W-379; E-33to W-379; E-34 to W-379; S-35 to W-379; L-36 to W-379;Y-37 to W-379; L-38 to W-379; W-39 to W-379; I-40 toW-379; D-41 to W-379; A-42 to W-379; H-43 to W-379;Q-44 to W-379; A-45 to W-379; R-46 to W-379; V-47 toW-379; L-48 to W-379; I-49 to W-379; G-50 to W-379; F-51to W-379; E-52 to W-379; E-53 to W-379; D-54 to W-379;I-55 to W-379; L-56 to W-379; I-57 to W-379; V-58 toW-379; S-59 to W-379; E-60 to W-379; G-61 to W-379; K-62to W-379; M-63 to W-379; A-64 to W-379; P-65 to W-379;F-66 to W-379; T-67 to W-379; H-68 to W-379; D-69 toW-379; F-70 to W-379; R-71 to W-379; K-72 to W-379; A-73to W-379; Q-74 to W-379; Q-75 to W-379; R-76 to W-379;M-77 to W-379; P-78 to W-379; A-79 to W-379; I-80 toW-379; P-81 to W-379; V-82 to W-379; N-83 to

W-379; I-84to W-379; H-85 to W-379; S-86 to W-379; M-87 to W-379;N-88 to W-379; F-89 to W-379; T-90 to W-379; W-91 toW-379; Q-92 to W-379; A-93 to W-379; A-94 to W-379;G-95 to W-379; Q-96 to W-379; A-97 to W-379; E-98 toW-379; Y-99 to W-379; F-100 to W-379; Y-101 to W-379;E-102 to W-379; F-103 to W-379; L-104 to W-379; S-105 toW-379; L-106 to W-379; R-107 to W-379; S-108 to W-379;L-109 to W-379; D-110 to W-379; K-111 to W-379; G-112 toW-379; I-113 to W-379; M-114 to W-379; A-115 to W-379;D-116 to W-379; P-117 to W-379; T-118 to W-379; V-119 toW-379; N-120 to W-379; V-121 to W-379; P-122 to W-379;L-123 to W-379; L-124 to W-379; G-125 to W-379; T-126 toW-379; V-127 to W-379; P-128 to W-379; H-129 to W-379;K-130 to W-379; A-131 to W-379; S-132 to W-379; V-133 toW-379; V-134 to W-379; Q-135 to W-379; V-136 to W-379;G-137 to W-379; F-138 to W-379; P-139 to W-379; C-140 toW-379; L-141 to W-379; G-142 to W-379; K-143 to W-379;Q-144 to W-379; D-145 to W-379; G-146 to W-379; V-147 toW-379; A-148 to W-379; A-149 to W-379; F-150 to W-379;E-151 to W-379; V-152 to W-379; D-153 to W-379; V-154 toW-379; I-155 to W-379; V-156 to W-379; M-157 to W-379;N-158 to W-379; S-159 to W-379; E-160 to W-379; G-161 toW-379; N-162 to W-379; T-163 to W-379; I-164 to W-379;L-165 to W-379; Q-166 to W-379; T-167 to W-379; P-168 toW-379; Q-169 to W-379; N-170 to W-379; A-171 to W-379;I-172 to W-379; F-173 to W-379; F-174 to W-379; K-175 toW-379; T-176 to W-379; C-177 to W-379; Q-178 to W-379;Q-179 to W-379; A-180 to W-379; E-181 to W-379; C-182 toW-379; P-183 to W-379; G-184 to W-379; G-185 to W-379;C-186 to W-379; R-187 to W-379; N-188 to W-379; G-189 toW-379; G-190 to W-379; F-191 to W-379; C-192 to W-379;N-193 to W-379; E-194 to W-379; R-195 to W-379; R-196 toW-379; I-197 to W-379; C-198 to W-379; E-199 to W-379;C-200 to W-379; P-201 to W-379; D-202 to W-379; G-203 toW-379; F-204 to W-379; H-205 to W-379; G-206 to W-379;P-207 to W-379; H-208 to W-379; C-209 to W-379; E-210 toW-379; K-211 to W-379; A-212 to W-379; L-213 to W-379;C-214 to W-379; T-215 to W-379; P-216 to W-379; R-217 toW-379; C-218 to W-379; M-219 to W-379; N-220 to W-379;G-221 to W-379; G-222 to W-379; L-223 to W-379; C-224 toW-379; V-225 to W-379; T-226 to W-379; P-227 to W-379;G-228 to W-379; F-229 to W-379; C-230 to W-379; I-231 toW-379; C-232 to W-379; P-233 to W-379; P-234 to W-379;G-235 to W-379; F-236 to W-379; Y-237 to W-379; G-238 toW-379; V-

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239 to W-379; N-240 to W-379; C-241 to W-379;D-242 to W-379; K-243 to W-379; A-244 to W-379; N-245 toW-379; C-246 to W-379; S-247 to W-379; T-248 to W-379;T-249 to W-379; C-250 to W-379; F-251 to W-379; N-252 toW-379; G-253 to W-379; G-254 to W-379; T-255 to W-379;C-256 to W-379; F-257 to W-379; Y-258 to W-379; P-259 toW-379; G-260 to W-379; K-261 to W-379; C-262 to W-379;I-263 to W-379; C-264 to W-379; P-265 to W-379; P-266 toW-379; G-267 to W-379; L-268 to W-379; E-269 to W-379;G-270 to W-379; E-271 to W-379; Q-272 to W-379; C-273 toW-379; E-274 to W-379; I-275 to W-379; S-276 to W-379;K-277 to W-379; C-278 to W-379; P-279 to W-379; Q-280 toW-379; P-281 to W-379; C-282 to W-379; R-283 to W-379;N-284 to W-379; G-285 to W-379; G-286 to W-379; K-287 toW-379; C-288 to W-379; I-289 to W-379; G-290 to W-379;K-291 to W-379; S-292 to W-379; K-293 to W-379; C-294 toW-379; K-295 to W-379; C-296 to W-379; S-297 to W-379;K-298 to W-379; G-299 to W-379; Y-300 to W-379; Q-301 toW-379; G-302 to W-379; D-303 to W-379; L-304 to W-379;C-305 to W-379; S-306 to W-379; K-307 to W-379; P-308 toW-379; V-309 to W-379; C-310 to W-379; E-311 to W-379;P-312 to W-379; G-313 to W-379; C-314 to W-379; G-315 toW-379; A-316 to W-379; H-317 to W-379; G-318 to W-379;T-319 to W-379; C-320 to W-379; H-321 to W-379; E-322 toW-379; P-323 to W-379; N-324 to W-379; K-325 to W-379;C-326 to W-379; Q-327 to W-379; C-328 to W-379; Q-329 toW-379; E-330 to W-379; G-331 to W-379; W-332 to W-379;H-333 to W-379; G-334 to W-379; R-335 to W-379; H-336 toW-379; C-337 to W-379; N-338 to W-379; K-339 to W-379;R-340 to W-379; Y-341 to W-379; E-342 to W-379; A-343 toW-379; S-344 to W-379; L-345 to W-379; I-346 to W-379;H-347 to W-379; A-348 to W-379; L-349 to W-379; R-350 toW-379; P-351 to W-379; A-352 to W-379; G-353 to W-379;A-354 to W-379; Q-355 to W-379; L-356 to W-379; R-357 toW-379; Q-358 to W-379; H-359 to W-379; T-360 to W-379;P-361 to W-379; S-362 to W-379; L-363 to W-379; K-364 toW-379; K-365 to W-379; A-366 to W-379; E-367 to W-379;E-368 to W-379; R-369 to W-379; R-370 to W-379; D-371 toW-379; P-372 to W-379; P-373 to W-379; and E-374 to W-379 of SEQ ID NO: 441. Polypeptides encoded by these polynucleotides are also encompassed by the invention. Moreover, fragments and variants of these polypeptides (such as, for example, fragments as described herein, polypeptides at least 80%, 85%, 90%, 95%, 96%, 97%, 98%, or 99% identical to

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these polypeptides and polypeptides encoded by the polynucleotide which hybridizes, under stringent conditions, to the polynucleotide encoding these polypeptides , or the complement there of are encompassed by the invention. Antibodies that bind polypeptides of the invention are also encompassed by the invention. Polynucleotides encoding these polypeptides are also encompassed by the invention.

Also as mentioned above, even if deletion of one or more amino acids from the C-terminus of a protein results in modification of loss of one or more biological functions of the protein, other functional activities (e.g., biological activities, ability to multimerize, ability to bind ligand, ability to generate antibodies, ability to bind antibodies) may still be retained. For example the ability of the shortened polypeptide to induce and/or bind to antibodies which recognize the complete or mature forms of the polypeptide generally will be retained when less than the majority of the residues of the complete or mature polypeptide are removed from the C-terminus. Whether a particular polypeptide lacking C-terminal residues of a complete polypeptide retains such immunologic activities can readily be determined by routine methods described herein and otherwise known in the art. It is not unlikely that a polypeptide with a large number of deleted C-terminal amino acid residues may retain some biological or immunogenic activities. In fact, peptides composed of as few as six amino acid residues may often evoke an immune response.

Accordingly, the present invention further provides polypeptides having one or more residues deleted from the carboxy terminus of the amino acid sequence of the polypeptide shown in SEQ ID NO:441, as described by the general formula 1-n, where n is an integer from 6 to 378, where n corresponds to the position of the amino acid residue identified in SEQ ID NO:441. More in particular, the invention provides polynucleotides encoding polypeptides comprising, or alternatively consisting of, an amino acid sequence selected from the group: M-1 toI-378; M-1 to Y-377; M-1 to N-376; M-1 to S-375; M-1 toE-374; M-1 to P-373; M-1 to P-372; M-1 to D-371; M-1 toR-370; M-1 to R-369; M-1 to E-368; M-1 to E-367; M-1 toA-366; M-1 to K-365; M-1 to K-364; M-1 to L-363; M-1 toS-362; M-1 to P-361; M-1 to T-360; M-1 to H-359; M-1 toQ-358; M-1 to R-357; M-1 to L-356; M-1 to Q-355; M-1 toA-354; M-1 to G-353; M-1 to A-352; M-1 to P-351; M-1 toR-350; M-1 to L-349; M-1 to A-348; M-

1 to H-347; M-1 toI-346; M-1 to L-345; M-1 to S-344; M-1 to A-343; M-1 toE-342; M-1 to Y-341; M-1 to R-340; M-1 to K-339; M-1 toN-338; M-1 to C-337; M-1 to H-336; M-1 to R-335; M-1 toG-334; M-1 to H-333; M-1 to W-332; M-1 to G-331; M-1 toE-330; M-1 to Q-329; M-1 to C-328; M-1 to Q-327; M-1 toC-326; M-1 to K-325; M-1 to N-324; M-1 to P-323; M-1 toE-322; M-1 to H-321; M-1 to C-320; M-1 to T-319; M-1 toG-318; M-1 to H-317; M-1 to A-316; M-1 to G-315; M-1 toC-314; M-1 to G-313; M-1 to P-312; M-1 to E-311; M-1 toC-310; M-1 to V-309; M-1 to P-308; M-1 to K-307; M-1 toS-306; M-1 to C-305; M-1 to L-304; M-1 to D-303; M-1 toG-302; M-1 to Q-301; M-1 to Y-300; M-1 to G-299; M-1 toK-298; M-1 to S-297; M-1 to C-296; M-1 to K-295; M-1 toC-294; M-1 to K-293; M-1 to S-292; M-1 to K-291; M-1 toG-290; M-1 to I-289; M-1 to C-288; M-1 to K-287; M-1 toG-286; M-1 to G-285; M-1 to N-284; M-1 to R-283; M-1 toC-282; M-1 to P-281; M-1 to Q-280; M-1 to P-279; M-1 toC-278; M-1 to K-277; M-1 to S-276; M-1 to I-275; M-1 toE-274; M-1 to C-273; M-1 to Q-272; M-1 to E-271; M-1 toG-270; M-1 to E-269; M-1 to L-268; M-1 to G-267; M-1 toP-266; M-1 to P-265; M-1 to C-264; M-1 to I-263; M-1 toC-262; M-1 to K-261; M-1 to G-260; M-1 to P-259; M-1 toY-258; M-1 to F-257; M-1 to C-256; M-1 to T-255; M-1 toG-254; M-1 to G-253; M-1 to N-252; M-1 to F-251; M-1 toC-250; M-1 to T-249; M-1 to T-248; M-1 to S-247; M-1 toC-246; M-1 to N-245; M-1 to A-244; M-1 to K-243; M-1 toD-242; M-1 to C-241; M-1 to N-240; M-1 to V-239; M-1 toG-238; M-1 to Y-237; M-1 to F-236; M-1 to G-235; M-1 toP-234; M-1 to P-233; M-1 to C-232; M-1 to I-231; M-1 toC-230; M-1 to F-229; M-1 to G-228; M-1 to P-227; M-1 toT-226; M-1 to V-225; M-1 to C-224; M-1 to L-223; M-1 toG-222; M-1 to G-221; M-1 to N-220; M-1 to M-219; M-1 toC-218; M-1 to R-217; M-1 to P-216; M-1 to T-215; M-1 toC-214; M-1 to L-213; M-1 to A-212; M-1 to K-211; M-1 toE-210; M-1 to C-209; M-1 to H-208; M-1 to P-207; M-1 toG-206; M-1 to H-205; M-1 to F-204; M-1 to G-203; M-1 toD-202; M-1 to P-201; M-1 to C-200; M-1 to E-199; M-1 toC-198; M-1 to I-197; M-1 to R-196; M-1 to R-195; M-1 toE-194; M-1 to N-193; M-1 to C-192; M-1 to F-191; M-1 toG-190; M-1 to G-189; M-1 to N-188; M-1 to R-187; M-1 toC-186; M-1 to G-185; M-1 to G-184; M-1 to P-183; M-1 toC-182; M-1 to E-181; M-1 to A-180; M-1 to Q-179; M-1 toQ-178; M-1 to C-177; M-1 to T-176; M-1 to K-175; M-1 toF-174; M-1 to F-173; M-1 to I-172; M-1 to A-171; M-1 toN-170; M-1 to Q-169; M-1 to P-168; M-1 to T-167; M-1 toQ-166; M-1 to

L-165; M-1 to I-164; M-1 to T-163; M-1 toN-162; M-1 to G-161; M-1 to E-160; M-1 to S-159; M-1 toN-158; M-1 to M-157; M-1 to V-156; M-1 to I-155; M-1 toV-154; M-1 to D-153; M-1 to V-152; M-1 to E-151; M-1 toF-150; M-1 to A-149; M-1 to A-148; M-1 to V-147; M-1 toG-146; M-1 to D-145; M-1 to Q-144; M-1 to K-143; M-1 toG-142; M-1 to L-141; M-1 to C-140; M-1 to P-139; M-1 toF-138; M-1 to G-137; M-1 to V-136; M-1 to Q-135; M-1 toV-134; M-1 to V-133; M-1 to S-132; M-1 to A-131; M-1 toK-130; M-1 to H-129; M-1 to P-128; M-1 to V-127; M-1 toT-126; M-1 to G-125; M-1 to L-124; M-1 to L-123; M-1 toP-122; M-1 to V-121; M-1 to N-120; M-1 to V-119; M-1 toT-118; M-1 to P-117; M-1 to D-116; M-1 to A-115; M-1 toM-114; M-1 to I-113; M-1 to G-112; M-1 to K-111; M-1 toD-110; M-1 to L-109; M-1 to S-108; M-1 to R-107; M-1 toL-106; M-1 to S-105; M-1 to L-104; M-1 to F-103; M-1 toE-102; M-1 to Y-101; M-1 to F-100; M-1 to Y-99; M-1 toE-98; M-1 to A-97; M-1 to Q-96; M-1 to G-95; M-1 to A-94;M-1 to A-93; M-1 to Q-92; M-1 to W-91; M-1 to T-90; M-1to F-89; M-1 to N-88; M-1 to M-87; M-1 to S-86; M-1 toH-85; M-1 to I-84; M-1 to N-83; M-1 to V-82; M-1 to P-81;M-1 to I-80; M-1 to A-79; M-1 to P-78; M-1 to M-77; M-1 toR-76; M-1 to Q-75; M-1 to Q-74; M-1 to A-73; M-1 to K-72;M-1 to R-71; M-1 to F-70; M-1 to D-69; M-1 to H-68; M-1 toT-67; M-1 to F-66; M-1 to P-65; M-1 to A-64; M-1 to M-63;M-1 to K-62; M-1 to G-61; M-1 to E-60; M-1 to S-59; M-1 toV-58; M-1 to I-57; M-1 to L-56; M-1 to I-55; M-1 to D-54;M-1 to E-53; M-1 to E-52; M-1 to F-51; M-1 to G-50; M-1 toI-49; M-1 to L-48; M-1 to V-47; M-1 to R-46; M-1 to A-45;M-1 to Q-44; M-1 to H-43; M-1 to A-42; M-1 to D-41; M-1to I-40; M-1 to W-39; M-1 to L-38; M-1 to Y-37; M-1 toL-36; M-1 to S-35; M-1 to E-34; M-1 to E-33; M-1 to Q-32;M-1 to P-31; M-1 to P-30; M-1 to G-29; M-1 to A-28; M-1 toE-27; M-1 to A-26; M-1 to R-25; M-1 to L-24; M-1 to A-23;M-1 to L-22; M-1 to L-21; M-1 to C-20; M-1 to L-19; M-1 toL-18; M-1 to I-17; M-1 to S-16; M-1 to W-15; M-1 to L-14;M-1 to W-13; M-1 to L-12; M-1 to A-11; M-1 to A-10; M-1to A-9; M-1 to P-8; M-1 to F-7; and M-1 to A-6 of SEQ ID NO:441. Polypeptides encoded by these polynucleotides are also encompassed by the invention. Moreover, fragments and variants of these polypeptides (such as, for example, fragments as described herein, polypeptides at least 80%, 85%, 90%, 95%, 96%, 97%, 98%, or 99% identical to these polypeptides and polypeptides encoded by the polynucleotide which hybridizes, under stringent conditions, to the polynucleotide encoding these

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polypeptides , or the complement there of are encompassed by the invention. Antibodies that bind polypeptides of the invention are also encompassed by the invention. Polynucleotides encoding these polypeptides are also encompassed by the invention.

The tissue distribution in brain and lung, combined with the homology to tenascin indicates that the protein product of this gene is useful for diagnosis and treatment of cancers. Alternatively, given the tissue distribution indicated by Northern analysis, the translation product of this gene is thought to be a growth factor functioning in the brain and lung that may be useful in treating neurodegeneration and lung disorder. For example, the protein product of this gene is useful for the detection and treatment of disorders associated with developing lungs, particularly in premature infants where the lungs are the last tissues to develop. Furthermore, the tissue distribution indicates that the protein product of this gene is useful for the diagnosis and intervention of lung tumors, since the gene may be involved in the regulation of cell division. Additionally, expression in the brain indicates that it may be involved in neuronal survival; synapse formation; conductance; neural differentiation, etc. Such involvement may impact many processes, such as learning and cognition. It may also be useful in the treatment of such neurodegenerative disorders as schizophrenia; ALS; or Alzheimer's.

Polynucleotides and polypeptides corresponding to this gene are useful for the treatment and diagnosis of hematopoietic related disorders such as anemia, pancytopenia, leukopenia, thrombocytopenia or leukemia since stromal cells are important in the production of cells of hematopoietic lineages. Representative uses are described in the "Immune Activity" and "Infectious Disease" sections below, in Example 11, 13, 14, 16, 18, 19, 20, and 27, and elsewhere herein. Briefly, the uses include bone marrow cell ex-vivo culture, bone marrow transplantation, bone marrow reconstitution, radiotherapy or chemotherapy of neoplasia. The gene product may also be involved in lymphopoiesis, therefore, it can be used in immune disorders such as infection, inflammation, allergy, immunodeficiency etc. In addition, this gene product may have commercial utility in the expansion of stem cells and committed progenitors of various blood lineages, and in the differentiation and/or proliferation of various cell types.

Protein, as well as, antibodies directed against the protein may show utility as a tissue-specific marker and/or immunotherapy target for the above listed tissues.

Many polynucleotide sequences, such as EST sequences, are publicly available and accessible through sequence databases. Some of these sequences are related to SEQ ID NO:203 and may have been publicly available prior to conception of the present invention. Preferably, such related polynucleotides are specifically excluded from the scope of the present invention. To list every related sequence is cumbersome. Accordingly, preferably excluded from the present invention are one or more polynucleotides comprising a nucleotide sequence described by the general formula of a-b, where a is any integer between 1 to 1960 of SEQ ID NO:203, b is an integer of 15 to 1974, where both a and b correspond to the positions of nucleotide residues shown in SEQ ID NO:203, and where b is greater than or equal to a + 14.

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FEATURES OF PROTEIN ENCODED BY GENE NO: 194

In specific embodiments, polypeptides of the invention comprise, or alternatively consists of, an amino acid sequence selected from the group: MNSAAGFSHLDRRERVLKLGESFEKQPRCASTLC (SEQ ID NO:1203). Moreover, fragments and variants of these polypeptides (such as, for example, fragments as described herein, polypeptides at least 80%, 85%, 90%, 95%, 96%, 97%, 98%, or 99% identical to these polypeptides and polypeptides encoded by the polynucleotide which hybridizes, under stringent conditions, to the polynucleotide encoding these polypeptides) are encompassed by the invention. Antibodies that bind polypeptides of the invention are also encompassed by the invention. Polynucleotides encoding these polypeptides are also encompassed by the invention.

This gene is expressed primarily in fetal human lung and neutrophils.

Polynucleotides and polypeptides of the invention are useful as reagents for differential identification of the tissue(s) or cell type(s) present in a biological sample and for diagnosis of diseases and conditions which include, but are not limited to, lung development and respiratory disorders. Similarly, polypeptides and antibodies directed to these polypeptides are useful in providing immunological probes for

differential identification of the tissue(s) or cell type(s). For a number of disorders of the above tissues or cells, particularly of the respiratory system, expression of this gene at significantly higher or lower levels may be routinely detected in certain tissues or cell types (e.g. respiratory, immune, cancerous and wounded tissues) or bodily fluids (e.g., lymph, serum, plasma, urine, synovial fluid and spinal fluid) or another tissue or cell sample taken from an individual having such a disorder, relative to the standard gene expression level, i.e., the expression level in healthy tissue or bodily fluid from an individual not having the disorder.

The tissue distribution in fetal lung and neutrophils indicates that the protein product of this gene is useful for the diagnosis and treatment of lung and immunity related diseases, for example, lung cancer, viral, fungal or bacterial infections (e.g. lesions caused by tuberculosis), inflammation (e.g. pneumonia), metabolic lesions etc. Furthermore, the tissue distribution indicates that the protein product of this gene is useful for the detection and treatment of disorders associated with developing lungs, particularly in premature infants where the lungs are the last tissues to develop. The tissue distribution indicates that the protein product of this gene is useful for the diagnosis and intervention of lung tumors, since the gene may be involved in the regulation of cell division, particularly since it is expressed in fetal tissue. Protein, as well as, antibodies directed against the protein may show utility as a tumor marker and immunotherapy targets for the above listed tumors and tissues.

Many polynucleotide sequences, such as EST sequences, are publicly available and accessible through sequence databases. Some of these sequences are related to SEQ ID NO:204 and may have been publicly available prior to conception of the present invention. Preferably, such related polynucleotides are specifically excluded from the scope of the present invention. To list every related sequence is cumbersome. Accordingly, preferably excluded from the present invention are one or more polynucleotides comprising a nucleotide sequence described by the general formula of a-b, where a is any integer between 1 to 1043 of SEQ ID NO:204, b is an integer of 15 to 1057, where both a and b correspond to the positions of nucleotide residues shown in SEQ ID NO:204, and where b is greater than or equal to a + 14.

FEATURES OF PROTEIN ENCODED BY GENE NO: 195

This gene is expressed primarily in breast lymph node, and to a lesser extent in synovial tissues.

Polynucleotides and polypeptides of the invention are useful as reagents for differential identification of the tissue(s) or cell type(s) present in a biological sample and for diagnosis of diseases and conditions which include, but are not limited to, immune and skeletal disorders. Similarly, polypeptides and antibodies directed to these polypeptides are useful in providing immunological probes for differential identification of the tissue(s) or cell type(s). For a number of disorders of the above tissues or cells, particularly of the immune system and skeletal system, expression of this gene at significantly higher or lower levels may be routinely detected in certain tissues or cell types (e.g. immune, skeletal, cancerous and wounded tissues) or bodily fluids (e.g., lymph, serum, plasma, urine, synovial fluid and spinal fluid) or another tissue or cell sample taken from an individual having such a disorder, relative to the standard gene expression level, i.e., the expression level in healthy tissue or bodily fluid from an individual not having the disorder.

The tissue distribution in breast lymph node and synovium indicates that the protein product of this gene is useful for the diagnosis and treatment of immune and skeletal disorders. Furthermore, this gene product may be involved in the regulation of cytokine production, antigen presentation, or other processes that may also suggest a usefulness in the treatment of cancer (e.g. by boosting immune responses). Since the gene is expressed in cells of lymphoid origin, the gene or protein, as well as, antibodies directed against the protein may show utility as a tumor marker and/or immunotherapy targets for the above listed tissues. Therefore it may be also used as an agent for immunological disorders including arthritis, asthma, immune deficiency diseases such as AIDS, leukemia, rheumatoid arthritis, inflammatory bowel disease, sepsis, acne, and psoriasis. In addition, this gene product may have commercial utility in the expansion of stem cells and committed progenitors of various blood lineages, and in the differentiation and/or proliferation of various cell types. Protein, as well as, antibodies directed against the protein may show utility as a tumor marker and/or immunotherapy targets for the above listed tissues. The expression of this

gene product in synovium indicates a role in the detection and treatment of disorders and conditions affecting the skeletal system, in particular osteoporosis as well as disorders afflicting connective tissues (e.g. arthritis, trauma, tendonitis, chrondomalacia and inflammation), such as in the diagnosis or treatment of various autoimmune disorders such as rheumatoid arthritis, lupus, scleroderma, and dermatomyositis as well as dwarfism, spinal deformation, and specific joint abnormalities as well as chondrodysplasias (i.e. spondyloepiphyseal dysplasia congenita, familial osteoarthritis, Atelosteogenesis type II, metaphyseal chondrodysplasia type Schmid). Protein, as well as, antibodies directed against the protein may show utility as a tumor marker and/or immunotherapy targets for the above listed tissues.

Many polynucleotide sequences, such as EST sequences, are publicly available and accessible through sequence databases. Some of these sequences are related to SEQ ID NO:205 and may have been publicly available prior to conception of the present invention. Preferably, such related polynucleotides are specifically excluded from the scope of the present invention. To list every related sequence is cumbersome. Accordingly, preferably excluded from the present invention are one or more polynucleotides comprising a nucleotide sequence described by the general formula of a-b, where a is any integer between 1 to 707 of SEQ ID NO:205, b is an integer of 15 to 721, where both a and b correspond to the positions of nucleotide residues shown in SEQ ID NO:205, and where b is greater than or equal to a + 14.

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FEATURES OF PROTEIN ENCODED BY GENE NO: 196

The gene encoding the disclosed cDNA is thought to reside on chromosome 5. Accordingly, polynucleotides related to this invention are useful as a marker in linkage analysis for chromosome 5. The translation product of this gene shares sequence homology with human M-phase phosphoprotein 4, which is thought to be important in the phosphorylation and signal transduction processes.

In specific embodiments, polypeptides of the invention comprise, or alternatively consists of, an amino acid sequence selected from the group:

TIYPTEEELQAVQKIVSITERALKLVSD (SEQ ID NO:1204), RALKGVLRVGVLAKGLLLRGDRNVNLVLLC (SEQ ID NO:1205), ALAALRHAKWFQARANGLQSCVIIIRILRDLCQRVPTWS (SEQ ID NO:1206), GDALRRVFECISSGIIL (SEQ ID NO:1207), LAFRQIHKVLGMDPLP (SEQ ID NO:1208), and/or TIYPTEEELQAVQKIVSITERALKLVSDSLSEHEKNKNKEGDDKKEGGKDRAL KGVLRVGVLAKGLLLRGDRNVNLVLLCSEKPSKTLLSRIAENLPKQLAVISPE KYDIKCAVSEAAIILNSCVEPKMQVTITLTSPIIREENMREGDVTSGMVKDPPD VLDRQKCLDALAALRHAKWFQARANGLQSCVIIIRILRDLCQRVPTWSDFPS WAMELLVEKAISSASSPQSPGDALRRVFECISSGIILKGSPGLLDPCEKDPFDTL ATMTDQQREDITSSAQFALRLLAFRQIHKVLGMDPLPQMSQRFNIHNNRKRR RDSDGVDGFEAEGKKDKKDYDNF (SEQ ID NO:1209), MERHPKKKMCSD (SEQ ID NO:1210), and/or GENSSSDFFPLFLFYFLVALASPPIFVSFIN (SEQ ID NO:1211). Moreover, fragments and variants of these polypeptides (such as, for example, fragments as described herein, polypeptides at least 80%, 85%, 90%, 95%, 96%, 97%, 98%, or 99% identical to these polypeptides and polypeptides encoded by the polynucleotide which hybridizes, under stringent conditions, to the polynucleotide encoding these polypeptides) are encompassed by the invention. Antibodies that bind polypeptides of the invention are also encompassed by the invention. Polynucleotides encoding these polypeptides are also encompassed by the invention.

This gene is expressed primarily in human hippocampus, and to a lesser extent in prostate and human frontal cortex.

Polynucleotides and polypeptides of the invention are useful as reagents for differential identification of the tissue(s) or cell type(s) present in a biological sample and for diagnosis of diseases and conditions which include, but are not limited to, disorders related to the reproductive and nervous systems. Similarly, polypeptides and antibodies directed to these polypeptides are useful in providing immunological probes for differential identification of the tissue(s) or cell type(s). For a number of disorders of the above tissues or cells, particularly of the reproductive and nervous systems, expression of this gene at significantly higher or lower levels may be routinely detected in certain tissues or cell types (e.g. reproductive, CNS, cancerous and wounded tissues) or bodily fluids (e.g., lymph, serum, plasma, urine, synovial

fluid and spinal fluid) or another tissue or cell sample taken from an individual having such a disorder, relative to the standard gene expression level, i.e., the expression level in healthy tissue or bodily fluid from an individual not having the disorder.

Predicted epitopes include those comprising a sequence shown in SEQ ID NO: 444 as residues: Arg-13 to Asp-21, Lys-28 to Lys-38, Val-76 to Asp-81, Ser-99 to Ala-107, Pro-130 to Phe-136, Thr-143 to Ile-150, Pro-176 to Phe-182, Asn-186 to Gly-196, Ala-202 to Phe-214.

The tissue distribution in human hippocampus, prostate, and frontal cortex, combined with the homology to human M-phase phosphoprotein 4 indicates that the protein product of this gene is useful for the diagnosis and treatment of reproductive and nervous system disorders. Furthermore, elevated expression of this gene product within the frontal cortex of the brain indicates that it may be involved in neuronal survival; synapse formation; conductance; neural differentiation, etc. Such involvement may impact many processes, such as learning and cognition. It may also be useful in the treatment of such neurodegenerative disorders as schizophrenia; ALS; or Alzheimer's. Protein, as well as, antibodies directed against the protein may show utility as a tissue-specific marker and/or immunotherapy target for the above listed tissues.

Many polynucleotide sequences, such as EST sequences, are publicly available and accessible through sequence databases. Some of these sequences are related to SEQ ID NO:206 and may have been publicly available prior to conception of the present invention. Preferably, such related polynucleotides are specifically excluded from the scope of the present invention. To list every related sequence is cumbersome. Accordingly, preferably excluded from the present invention are one or more polynucleotides comprising a nucleotide sequence described by the general formula of a-b, where a is any integer between 1 to 2451 of SEQ ID NO:206, b is an integer of 15 to 2465, where both a and b correspond to the positions of nucleotide residues shown in SEQ ID NO:206, and where b is greater than or equal to a + 14.

FEATURES OF PROTEIN ENCODED BY GENE NO: 197

In specific embodiments, polypeptides of the invention comprise, or alternatively consists of, an amino acid sequence selected from the group: MGSQHSAAARPSSCRRKQEDDRDG (SEQ ID NO:1212), LLAEREQEEAIAQFPYVEFTGRDSITCLTC (SEQ ID NO:1213), and/or QGTGYIPTEQVNELVALI PHSDQRLRPQRTKQYV (SEQ ID NO:1214). Moreover, fragments and variants of these polypeptides (such as, for example, fragments as described herein, polypeptides at least 80%, 85%, 90%, 95%, 96%, 97%, 98%, or 99% identical to these polypeptides and polypeptides encoded by the polynucleotide which hybridizes, under stringent conditions, to the polynucleotide encoding these polypeptides) are encompassed by the invention. Antibodies that bind polypeptides of the invention are also encompassed by the invention. Polynucleotides encoding these polypeptides are also encompassed by the invention.

This gene is expressed primarily in human primary breast cancer, and to a lesser extent, in human adult spleen, Hodgkin's lymphoma I, and salivary gland.

Polynucleotides and polypeptides of the invention are useful as reagents for differential identification of the tissue(s) or cell type(s) present in a biological sample and for diagnosis of diseases and conditions which include, but are not limited to, cancer, as well as immune disorders. Similarly, polypeptides and antibodies directed to these polypeptides are useful in providing immunological probes for differential identification of the tissue(s) or cell type(s). For a number of disorders of the above tissues or cells, particularly cancers and the immune system, expression of this gene at significantly higher or lower levels may be routinely detected in certain tissues or cell types (e.g. immune, cancerous and wounded tissues) or bodily fluids (e.g., lymph, serum, plasma, urine, synovial fluid and spinal fluid) or another tissue or cell sample taken from an individual having such a disorder, relative to the standard gene expression level, i.e., the expression level in healthy tissue or bodily fluid from an individual not having the disorder.

Predicted epitopes include those comprising a sequence shown in SEQ ID NO: 445 as residues: Ser-126 to Gly-138.

The tissue distribution in tumors of breast origins indicates that the protein product of this gene is useful for the diagnosis and intervention of these tumors, in addition to other tumors where expression has been indicated. Furthermore, the

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expression in hematopoietic cells and tissues indicates that this protein may play a role in the proliferation, differentiation, and/or survival of hematopoietic cell lineages. In such an event, this gene may be useful in the treatment of lymphoproliferative disorders, and in the maintenance and differentiation of various hematopoietic lineages from early hematopoietic stem and committed progenitor cells. Protein, as well as, antibodies directed against the protein may show utility as a tissue-specific marker and/or immunotherapy target for the above listed tissues.

Many polynucleotide sequences, such as EST sequences, are publicly available and accessible through sequence databases. Some of these sequences are related to SEQ ID NO:207 and may have been publicly available prior to conception of the present invention. Preferably, such related polynucleotides are specifically excluded from the scope of the present invention. To list every related sequence is cumbersome. Accordingly, preferably excluded from the present invention are one or more polynucleotides comprising a nucleotide sequence described by the general formula of a-b, where a is any integer between 1 to 1466 of SEQ ID NO:207, b is an integer of 15 to 1480, where both a and b correspond to the positions of nucleotide residues shown in SEQ ID NO:207, and where b is greater than or equal to a + 14.

P4P0E2P0S0E0P0

FEATURES OF PROTEIN ENCODED BY GENE NO: 198

This gene is expressed primarily in monocytes.

Polynucleotides and polypeptides of the invention are useful as reagents for differential identification of the tissue(s) or cell type(s) present in a biological sample and for diagnosis of diseases and conditions which include, but are not limited to, blood cell disorders. Similarly, polypeptides and antibodies directed to these polypeptides are useful in providing immunological probes for differential identification of the tissue(s) or cell type(s). For a number of disorders of the above tissues or cells, particularly of the immune system, expression of this gene at significantly higher or lower levels may be routinely detected in certain tissues or cell types (e.g. immune, cancerous and wounded tissues) or bodily fluids (e.g., lymph, serum, plasma, urine, synovial fluid and spinal fluid) or another tissue or cell sample

taken from an individual having such a disorder, relative to the standard gene expression level, i.e., the expression level in healthy tissue or bodily fluid from an individual not having the disorder.

The tissue distribution in monocytes indicates that the protein product of this gene is useful for the diagnosis and treatment of blood cell disorders. Furthermore, expression of this gene product in monocytes also strongly indicates a role for this protein in immune function and immune surveillance. Protein, as well as, antibodies directed against the protein may show utility as a tumor marker and/or immunotherapy targets for the above listed tissues.

Many polynucleotide sequences, such as EST sequences, are publicly available and accessible through sequence databases. Some of these sequences are related to SEQ ID NO:208 and may have been publicly available prior to conception of the present invention. Preferably, such related polynucleotides are specifically excluded from the scope of the present invention. To list every related sequence is cumbersome. Accordingly, preferably excluded from the present invention are one or more polynucleotides comprising a nucleotide sequence described by the general formula of a-b, where a is any integer between 1 to 858 of SEQ ID NO:208, b is an integer of 15 to 872, where both a and b correspond to the positions of nucleotide residues shown in SEQ ID NO:208, and where b is greater than or equal to a + 14.

P0005WO00

FEATURES OF PROTEIN ENCODED BY GENE NO: 199

The gene encoding the disclosed cDNA is thought to reside on chromosome 6. Accordingly, polynucleotides related to this invention are useful as a marker in linkage analysis for chromosome 6.

This gene is expressed primarily in human ovary and synovia, and to a lesser extent in human 8 week whole embryo.

Polynucleotides and polypeptides of the invention are useful as reagents for differential identification of the tissue(s) or cell type(s) present in a biological sample and for diagnosis of diseases and conditions which include, but are not limited to, reproductive and developmental disorders. Similarly, polypeptides and antibodies

directed to these polypeptides are useful in providing immunological probes for differential identification of the tissue(s) or cell type(s). For a number of disorders of the above tissues or cells, particularly of the reproductive and developmental systems, expression of this gene at significantly higher or lower levels may be routinely detected in certain tissues or cell types (e.g. reproductive, developmental, cancerous and wounded tissues) or bodily fluids (e.g., lymph, serum, plasma, urine, synovial fluid and spinal fluid) or another tissue or cell sample taken from an individual having such a disorder, relative to the standard gene expression level, i.e., the expression level in healthy tissue or bodily fluid from an individual not having the disorder.

The tissue distribution in human ovary and human 8 week whole embryo indicates that the protein product of this gene is useful for the diagnosis and treatment of reproductive and developmental disorders. Similarly, expression within embryonic tissue and other cellular sources marked by proliferating cells indicates that this protein may play a role in the regulation of cellular division, and may show utility in the diagnosis and treatment of cancer and other proliferative disorders. Similarly, embryonic development also involves decisions involving cell differentiation and/or apoptosis in pattern formation. Thus this protein may also be involved in apoptosis or tissue differentiation and could again be useful in cancer therapy. Protein, as well as, antibodies directed against the protein may show utility as a tumor marker and/or immunotherapy targets for the above listed tissues.

Many polynucleotide sequences, such as EST sequences, are publicly available and accessible through sequence databases. Some of these sequences are related to SEQ ID NO:209 and may have been publicly available prior to conception of the present invention. Preferably, such related polynucleotides are specifically excluded from the scope of the present invention. To list every related sequence is cumbersome. Accordingly, preferably excluded from the present invention are one or more polynucleotides comprising a nucleotide sequence described by the general formula of a-b, where a is any integer between 1 to 1765 of SEQ ID NO:209, b is an integer of 15 to 1779, where both a and b correspond to the positions of nucleotide residues shown in SEQ ID NO:209, and where b is greater than or equal to a + 14.

DC3_3676207.1

FEATURES OF PROTEIN ENCODED BY GENE NO: 200

The gene encoding the disclosed cDNA is thought to reside on chromosome 8. Accordingly, polynucleotides related to this invention are useful as a marker in linkage analysis for chromosome 8. The translation product of this gene shares limited sequence homology with collagen proline rich domain.

This gene is expressed primarily in CNS.

Polynucleotides and polypeptides of the invention are useful as reagents for differential identification of the tissue(s) or cell type(s) present in a biological sample and for diagnosis of diseases and conditions which include, but are not limited to, neurological diseases. Similarly, polypeptides and antibodies directed to these polypeptides are useful in providing immunological probes for differential identification of the tissue(s) or cell type(s). For a number of disorders of the above tissues or cells, particularly of the nervous system, expression of this gene at significantly higher or lower levels may be routinely detected in certain tissues or cell types (e.g. CNS, cancerous and wounded tissues) or bodily fluids (e.g., lymph, serum, plasma, urine, synovial fluid and spinal fluid) or another tissue or cell sample taken from an individual having such a disorder, relative to the standard gene expression level, i.e., the expression level in healthy tissue or bodily fluid from an individual not having the disorder.

Predicted epitopes include those comprising a sequence shown in SEQ ID NO: 448 as residues: Pro-35 to Asp-41.

The tissue distribution in tissues of the central nervous system indicates that the protein product of this gene is useful for the diagnosis and treatment of neurological diseases and disorders, such as Alzheimer's Disease, Parkinson's Disease, Huntington's Disease, Tourette's Syndrome, schizophrenia, mania, dementia, paranoia, obsessive compulsive disorder, panic disorder, learning disabilities, ALS, psychoses, autism, and altered behaviors, including disorders in feeding, sleep patterns, balance, and perception. In addition, the gene or gene product may also play a role in the treatment and/or detection of developmental disorders associated with the developing embryo, or sexually-linked disorders. Protein, as well as, antibodies

directed against the protein may show utility as a tumor marker and/or immunotherapy targets for the above listed tissues.

Many polynucleotide sequences, such as EST sequences, are publicly available and accessible through sequence databases. Some of these sequences are related to SEQ ID NO:210 and may have been publicly available prior to conception of the present invention. Preferably, such related polynucleotides are specifically excluded from the scope of the present invention. To list every related sequence is cumbersome. Accordingly, preferably excluded from the present invention are one or more polynucleotides comprising a nucleotide sequence described by the general formula of a-b, where a is any integer between 1 to 2096 of SEQ ID NO:210, b is an integer of 15 to 2110, where both a and b correspond to the positions of nucleotide residues shown in SEQ ID NO:210, and where b is greater than or equal to a + 14.

FEATURES OF PROTEIN ENCODED BY GENE NO: 201

The translation product of this gene shares homology with a mammalian histone H1a protein.

In specific embodiments, polypeptides of the invention comprise, or alternatively consists of, an amino acid sequence selected from the group: ARLNVGRESLKREMLKSQGVKVSESPMGARHSSWPEGAAFCKKVQGAQMQ FPPRR (SEQ ID NO:1215), ARLNVGRESLKREML (SEQ ID NO:1216), LKSQGV KVSESPMGARHSSW (SEQ ID NO:1217), AFCKKVQGAQMQFPPRR (SEQ ID NO:1218), and/or AFCKKVQGAQMQFPPRR (SEQ ID NO:1219). Moreover, fragments and variants of these polypeptides (such as, for example, fragments as described herein, polypeptides at least 80%, 85%, 90%, 95%, 96%, 97%, 98%, or 99% identical to these polypeptides and polypeptides encoded by the polynucleotide which hybridizes, under stringent conditions, to the polynucleotide encoding these polypeptides) are encompassed by the invention. Antibodies that bind polypeptides of the invention are also encompassed by the invention. Polynucleotides encoding these polypeptides are also encompassed by the invention. (See Genbank Accession No. pir|S24178).

This gene is expressed primarily in neutrophils.

Polynucleotides and polypeptides of the invention are useful as reagents for differential identification of the tissue(s) or cell type(s) present in a biological sample and for diagnosis of diseases and conditions which include, but are not limited to, immune disorders. Similarly, polypeptides and antibodies directed to these polypeptides are useful in providing immunological probes for differential identification of the tissue(s) or cell type(s). For a number of disorders of the above tissues or cells, particularly of the immune system, expression of this gene at significantly higher or lower levels may be routinely detected in certain tissues or cell types (e.g. immune, cancerous and wounded tissues) or bodily fluids (e.g., lymph, serum, plasma, urine, synovial fluid and spinal fluid) or another tissue or cell sample taken from an individual having such a disorder, relative to the standard gene expression level, i.e., the expression level in healthy tissue or bodily fluid from an individual not having the disorder.

The tissue distribution in neutrophils indicates that the protein product of this gene is useful for the diagnosis and treatment of immune disorders. Since the gene is expressed in cells of lymphoid origin, the natural gene product may be involved in vital immune functions. Therefore it may be also used as an agent for immunological disorders including arthritis, asthma, immune deficiency diseases such as AIDS, and leukemia. Furthermore, expression of this gene product in neutrophils also strongly indicates a role for this protein in immune function and immune surveillance. Protein, as well as, antibodies directed against the protein may show utility as a tumor marker and/or immunotherapy targets for the above listed tissues.

Many polynucleotide sequences, such as EST sequences, are publicly available and accessible through sequence databases. Some of these sequences are related to SEQ ID NO:211 and may have been publicly available prior to conception of the present invention. Preferably, such related polynucleotides are specifically excluded from the scope of the present invention. To list every related sequence is cumbersome. Accordingly, preferably excluded from the present invention are one or more polynucleotides comprising a nucleotide sequence described by the general formula of a-b, where a is any integer between 1 to 924 of SEQ ID NO:211, b is an

integer of 15 to 938, where both a and b correspond to the positions of nucleotide residues shown in SEQ ID NO:211, and where b is greater than or equal to a + 14.

FEATURES OF PROTEIN ENCODED BY GENE NO: 202

This gene is expressed primarily in neutrophils.

Polynucleotides and polypeptides of the invention are useful as reagents for differential identification of the tissue(s) or cell type(s) present in a biological sample and for diagnosis of diseases and conditions which include, but are not limited to, immune disorders. Similarly, polypeptides and antibodies directed to these polypeptides are useful in providing immunological probes for differential identification of the tissue(s) or cell type(s). For a number of disorders of the above tissues or cells, particularly of the immune system, expression of this gene at significantly higher or lower levels may be routinely detected in certain tissues or cell types (e.g. immune, cancerous and wounded tissues) or bodily fluids (e.g., lymph, serum, plasma, urine, synovial fluid and spinal fluid) or another tissue or cell sample taken from an individual having such a disorder, relative to the standard gene expression level, i.e., the expression level in healthy tissue or bodily fluid from an individual not having the disorder.

The tissue distribution in neutrophils indicates that the protein product of this gene is useful for the diagnosis and treatment of immune disorders. Since the gene is expressed in cells of lymphoid origin, the natural gene product may be involved in immune functions. Therefore it may be also used as an agent for immunological disorders including arthritis, asthma, immune deficiency diseases such as AIDS, and leukemia. Furthermore, expression of this gene product in neutrophils also strongly indicates a role for this protein in immune function and immune surveillance. Protein, as well as, antibodies directed against the protein may show utility as a tumor marker and/or immunotherapy targets for the above listed tissues.

Many polynucleotide sequences, such as EST sequences, are publicly available and accessible through sequence databases. Some of these sequences are related to SEQ ID NO:212 and may have been publicly available prior to conception

of the present invention. Preferably, such related polynucleotides are specifically excluded from the scope of the present invention. To list every related sequence is cumbersome. Accordingly, preferably excluded from the present invention are one or more polynucleotides comprising a nucleotide sequence described by the general formula of a-b, where a is any integer between 1 to 1537 of SEQ ID NO:212, b is an integer of 15 to 1551, where both a and b correspond to the positions of nucleotide residues shown in SEQ ID NO:212, and where b is greater than or equal to a + 14.

FEATURES OF PROTEIN ENCODED BY GENE NO: 203

This gene is expressed primarily in neutrophils.

Polynucleotides and polypeptides of the invention are useful as reagents for differential identification of the tissue(s) or cell type(s) present in a biological sample and for diagnosis of diseases and conditions which include, but are not limited to, infectious disorders, immune disorders, and cancers. Similarly, polypeptides and antibodies directed to these polypeptides are useful in providing immunological probes for differential identification of the tissue(s) or cell type(s). For a number of disorders of the above tissues or cells, particularly of the immune system, expression of this gene at significantly higher or lower levels may be routinely detected in certain tissues or cell types (e.g. immune, cancerous and wounded tissues) or bodily fluids (e.g., lymph, serum, plasma, urine, synovial fluid and spinal fluid) or another tissue or cell sample taken from an individual having such a disorder, relative to the standard gene expression level, i.e., the expression level in healthy tissue or bodily fluid from an individual not having the disorder.

Predicted epitopes include those comprising a sequence shown in SEQ ID NO: 451 as residues: Thr-31 to Lys-36.

The tissue distribution in neutrophils indicates that the protein product of this gene is useful for the diagnosis and treatment of infectious disorders, immune disorders, and cancers. Since the gene is expressed in cells of lymphoid origin, the natural gene product may be involved in immune functions. Therefore it may be also used as an agent for immunological disorders including arthritis, asthma, immune

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deficiency diseases such as AIDS, and leukemia. Expression of this gene product in neutrophils also strongly indicates a role for this protein in immune function and immune surveillance. Protein, as well as, antibodies directed against the protein may show utility as a tumor marker and/or immunotherapy targets for the above listed tissues.

Many polynucleotide sequences, such as EST sequences, are publicly available and accessible through sequence databases. Some of these sequences are related to SEQ ID NO:213 and may have been publicly available prior to conception of the present invention. Preferably, such related polynucleotides are specifically excluded from the scope of the present invention. To list every related sequence is cumbersome. Accordingly, preferably excluded from the present invention are one or more polynucleotides comprising a nucleotide sequence described by the general formula of a-b, where a is any integer between 1 to 983 of SEQ ID NO:213, b is an integer of 15 to 997, where both a and b correspond to the positions of nucleotide residues shown in SEQ ID NO:213, and where b is greater than or equal to a + 14.

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FEATURES OF PROTEIN ENCODED BY GENE NO: 204

The gene encoding the disclosed cDNA is thought to reside on chromosome 16. Accordingly, polynucleotides related to this invention are useful as a marker in linkage analysis for chromosome 16. The translation product of this gene shares sequence homology with lactate dehydrogenase, which is thought to be important in lactate metabolism.

This gene is expressed primarily in human tonsils, and to a lesser extent, in spleen, and neutrophils.

Polynucleotides and polypeptides of the invention are useful as reagents for differential identification of the tissue(s) or cell type(s) present in a biological sample and for diagnosis of diseases and conditions which include, but are not limited to, immune disorders, infectious disorders, and cancers. Similarly, polypeptides and antibodies directed to these polypeptides are useful in providing immunological probes for differential identification of the tissue(s) or cell type(s). For a number of

disorders of the above tissues or cells, particularly of the immune disorders, infectious disorders, and cancers, expression of this gene at significantly higher or lower levels may be routinely detected in certain tissues or cell types (e.g. tonsils, immune, cancerous and wounded tissues) or bodily fluids (e.g., lymph, serum, plasma, urine, synovial fluid and spinal fluid) or another tissue or cell sample taken from an individual having such a disorder, relative to the standard gene expression level, i.e., the expression level in healthy tissue or bodily fluid from an individual not having the disorder.

Predicted epitopes include those comprising a sequence shown in SEQ ID NO: 452 as residues: Gly-7 to Ser-12.

The tissue distribution in human tonsils, spleen, and neutrophils, combined with the homology to lactate dehydrogenase gene indicates that the protein product of this gene is useful for the diagnosis and treatment of immune disorders, infectious disorders, and cancers. Furthermore, expression of this gene product in tonsils indicates a role in the regulation of the proliferation; survival; differentiation; and/or activation of potentially all hematopoietic cell lineages, including blood stem cells. This gene product may be involved in the regulation of cytokine production, antigen presentation, or other processes that may also suggest a usefulness in the treatment of cancer (e.g. by boosting immune responses). Since the gene is expressed in cells of lymphoid origin, the gene or protein, as well as, antibodies directed against the protein may show utility as a tumor marker and/or immunotherapy targets for the above listed tissues. Therefore it may be also used as an agent for immunological disorders including arthritis, asthma, immune deficiency diseases such as AIDS, leukemia, rheumatoid arthritis, inflammatory bowel disease, sepsis, acne, and psoriasis. In addition, this gene product may have commercial utility in the expansion of stem cells and committed progenitors of various blood lineages, and in the differentiation and/or proliferation of various cell types. Protein, as well as, antibodies directed against the protein may show utility as a tumor marker and/or immunotherapy targets for the above listed tissues.

Many polynucleotide sequences, such as EST sequences, are publicly available and accessible through sequence databases. Some of these sequences are related to SEQ ID NO:214 and may have been publicly available prior to conception

of the present invention. Preferably, such related polynucleotides are specifically excluded from the scope of the present invention. To list every related sequence is cumbersome. Accordingly, preferably excluded from the present invention are one or more polynucleotides comprising a nucleotide sequence described by the general formula of a-b, where a is any integer between 1 to 1482 of SEQ ID NO:214, b is an integer of 15 to 1496, where both a and b correspond to the positions of nucleotide residues shown in SEQ ID NO:214, and where b is greater than or equal to a + 14.

FEATURES OF PROTEIN ENCODED BY GENE NO: 205

The translation product of this gene shares sequence homology with Gcap1 protein which is developmentally regulated in brain.

In specific embodiments, polypeptides of the invention comprise, or alternatively consists of, the following amino acid sequence: NFFFVCLFKSSLRLVNSSYTPILCVL (SEQ ID NO:1220). Moreover, fragments and variants of this polypeptide (such as, for example, fragments as described herein, polypeptides at least 80%, 85%, 90%, 95%, 96%, 97%, 98%, or 99% identical to these polypeptides and polypeptides encoded by the polynucleotide which hybridize, under stringent conditions, to the polynucleotide encoding this polypeptide are encompassed by the invention. Antibodies that bind polypeptides of the invention are also encompassed by the invention. Polynucleotides encoding this polypeptide are also encompassed by the invention.

The gene encoding the disclosed cDNA is thought to reside on chromosome 7. Accordingly, polynucleotides related to this invention are useful as a marker in linkage analysis for chromosome 7.

This gene is expressed primarily in placenta and endometrial tumors.

Polynucleotides and polypeptides of the invention are useful as reagents for differential identification of the tissue(s) or cell type(s) present in a biological sample and for diagnosis of diseases and conditions which include, but are not limited to, vasculogenesis/angiogenesis and tumorigenesis. Similarly, polypeptides and

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antibodies directed to these polypeptides are useful in providing immunological probes for differential identification of the tissue(s) or cell type(s). For a number of disorders of the above tissues or cells, particularly of the vascular system and tumors, expression of this gene at significantly higher or lower levels may be routinely detected in certain tissues or cell types (e.g. placental, cancerous and wounded tissues) or bodily fluids (e.g., lymph, serum, plasma, urine, synovial fluid and spinal fluid) or another tissue or cell sample taken from an individual having such a disorder, relative to the standard gene expression level, i.e., the expression level in healthy tissue or bodily fluid from an individual not having the disorder.

Predicted epitopes include those comprising a sequence shown in SEQ ID NO: 453 as residues: Lys-9 to Gln-16.

The tissue distribution placenta and endometrial tumors, combined with the homology to Gcap1 protein indicates that the protein product of this gene is useful for the diagnosis and treatment of disorders or dysfunctions of the vascular system, which include, but are not limited to atherosclerosis, hypertension, embolism, thrombosis, microvascular disease, aneurysm, or stroke, or tumorigenesis. Furthermore, the tissue distribution indicates that the protein product of this gene is useful for the diagnosis and/or treatment of disorders of the placenta. Specific expression within the placenta indicates that this gene product may play a role in the proper establishment and maintenance of placental function. Alternately, this gene product may be produced by the placenta and then transported to the embryo, where it may play a crucial role in the development and/or survival of the developing embryo or fetus. Expression of this gene product in a vascular-rich tissue such as the placenta also indicates that this gene product may be produced more generally in endothelial cells or within the circulation. In such instances, it may play more generalized roles in vascular function, such as in angiogenesis. It may also be produced in the vasculature and have effects on other cells within the circulation, such as hematopoietic cells. It may serve to promote the proliferation, survival, activation, and/or differentiation of hematopoietic cells, as well as other cells throughout the body.

Many polynucleotide sequences, such as EST sequences, are publicly available and accessible through sequence databases. Some of these sequences are related to SEQ ID NO:215 and may have been publicly available prior to conception

of the present invention. Preferably, such related polynucleotides are specifically excluded from the scope of the present invention. To list every related sequence is cumbersome. Accordingly, preferably excluded from the present invention are one or more polynucleotides comprising a nucleotide sequence described by the general formula of a-b, where a is any integer between 1 to 1294 of SEQ ID NO:215, b is an integer of 15 to 1308, where both a and b correspond to the positions of nucleotide residues shown in SEQ ID NO:215, and where b is greater than or equal to a + 14.

FEATURES OF PROTEIN ENCODED BY GENE NO: 206

The translation product of this gene shares sequence homology with a C. elegans protein of unknown function (F23B2.4 [Caenorhabditis elegans]).

In specific embodiments, polypeptides of the invention comprise, or alternatively consist of, the following amino acid sequences: VQVLEQLTNNAVAESRFNDAAYYYWMLSMQCLDIAQD (SEQ ID NO:1221), PAQKDTMLGKFYHFQRLAELYHGYHAIHRHTEDP (SEQ ID NO:1222), LAKQSKALGAYRLARHAYDKLRGLYIP (SEQ ID NO:1223), ARFQKSIELGTLTIRAKPFHDSEELVPLCYRCSTNN (SEQ ID NO:1224), PLLNNLGNVCINCRQPFIFSASSYDVLHLVEFYLEEGITDEEAISLIDLEVLRPK RDDRQLEICKQQLPDSCG (SEQ ID NO:1225) MPYAQWLAENDRFEEAQKAFHKAGRQREA (SEQ ID NO:1226), and/or FSVHRPETLFNISRFLLHSLPKDTPSGISKVKILFT (SEQ ID NO:1227). Moreover, fragments and variants of these polypeptides (such as, for example, fragments as described herein, polypeptides at least 80%, 85%, 90%, 95%, 96%, 97%, 98%, or 99% identical to these polypeptides and polypeptides encoded by the polynucleotide which hybridizes, under stringent conditions, to the polynucleotide encoding these polypeptides) are encompassed by the invention. Antibodies that bind polypeptides of the invention are also encompassed by the invention. Polynucleotides encoding these polypeptides are also encompassed by the invention.

This gene is expressed primarily in testes.

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Polynucleotides and polypeptides of the invention are useful as reagents for differential identification of the tissue(s) or cell type(s) present in a biological sample and for diagnosis of diseases and conditions which include, but are not limited to, male reproductive and endocrine disorders. Similarly, polypeptides and antibodies directed to these polypeptides are useful in providing immunological probes for differential identification of the tissue(s) or cell type(s). For a number of disorders of the above tissues or cells, particularly of the reproductive and endocrine systems, expression of this gene at significantly higher or lower levels may be routinely detected in certain tissues or cell types (e.g. testes, cancerous and wounded tissues) or bodily fluids (e.g., lymph, serum, seminal fluid, plasma, urine, synovial fluid and spinal fluid) or another tissue or cell sample taken from an individual having such a disorder, relative to the standard gene expression level, i.e., the expression level in healthy tissue or bodily fluid from an individual not having the disorder.

The tissue distribution in testes indicates that the protein product of this gene is useful for the treatment of male reproductive and endocrine disorders. Furthermore, the tissue distribution indicates that the protein product of this gene is useful for the treatment and diagnosis of conditions concerning proper testicular function (e.g. endocrine function, sperm maturation), as well as cancer. Therefore, this gene product is useful in the treatment of male infertility and/or impotence. This gene product is also useful in assays designed to identify binding agents, as such agents (antagonists/agonists) are useful as male contraceptive agents. Similarly, the protein is believed to be useful in the treatment and/or diagnosis of testicular cancer. The testes are also a site of active gene expression of transcripts that may be expressed, particularly at low levels, in other tissues of the body. Therefore, this gene product may be expressed in other specific tissues or organs where it may play related functional roles in other processes, such as hematopoiesis, inflammation, bone formation, and kidney function, to name a few possible target indications.

Many polynucleotide sequences, such as EST sequences, are publicly available and accessible through sequence databases. Some of these sequences are related to SEQ ID NO:216 and may have been publicly available prior to conception of the present invention. Preferably, such related polynucleotides are specifically excluded from the scope of the present invention. To list every related sequence is

cumbersome. Accordingly, preferably excluded from the present invention are one or more polynucleotides comprising a nucleotide sequence described by the general formula of a-b, where a is any integer between 1 to 1691 of SEQ ID NO:216, b is an integer of 15 to 1705, where both a and b correspond to the positions of nucleotide residues shown in SEQ ID NO:216, and where b is greater than or equal to a + 14.

FEATURES OF PROTEIN ENCODED BY GENE NO: 207

This gene is expressed in fetal lung.

Polynucleotides and polypeptides of the invention are useful as reagents for differential identification of the tissue(s) or cell type(s) present in a biological sample and for diagnosis of diseases and conditions which include, but are not limited to, lung diseases such as cystic fibrosis. Similarly, polypeptides and antibodies directed to these polypeptides are useful in providing immunological probes for differential identification of the tissue(s) or cell type(s). For a number of disorders of the above tissues or cells, particularly of the respiratory system, expression of this gene at significantly higher or lower levels may be routinely detected in certain tissues or cell types (e.g. respiratory, cancerous and wounded tissues) or bodily fluids (e.g., serum, plasma, urine, synovial fluid and spinal fluid) or another tissue or cell sample taken from an individual having such a disorder, relative to the standard gene expression level, i.e., the expression level in healthy tissue or bodily fluid from an individual not having the disorder.

Predicted epitopes include those comprising a sequence shown in SEQ ID NO: 455 as residues: Tyr-49 to Cys-54.

The tissue distribution in fetal lung indicates that the protein product of this gene is useful for the detection and treatment of disorders associated with developing lungs, particularly in premature infants where the lungs are the last tissues to develop. The tissue distribution indicates that the protein product of this gene is useful for the diagnosis and intervention of lung tumors, since the gene may be involved in the regulation of cell division, particularly since it is expressed in fetal tissue. Protein, as

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well as, antibodies directed against the protein may show utility as a tumor marker and immunotherapy targets for the above listed tumors and tissues.

Many polynucleotide sequences, such as EST sequences, are publicly available and accessible through sequence databases. Some of these sequences are related to SEQ ID NO:217 and may have been publicly available prior to conception of the present invention. Preferably, such related polynucleotides are specifically excluded from the scope of the present invention. To list every related sequence is cumbersome. Accordingly, preferably excluded from the present invention are one or more polynucleotides comprising a nucleotide sequence described by the general formula of a-b, where a is any integer between 1 to 985 of SEQ ID NO:217, b is an integer of 15 to 999, where both a and b correspond to the positions of nucleotide residues shown in SEQ ID NO:217, and where b is greater than or equal to a + 14.

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T02280 "297EE60

Table 1

Gene No.	cDNA Clone ID	ATCC Deposit No:Z and Date	Vector	NT SEQ ID NO: X	Total NT Seq.	5' NT of Clone Seq.	3' NT of Clone Seq.	5' NT of Start Codon	5' NT of First AA of Signal Pep	AA SEQ ID NO: Y	First AA of Sig Pep	Last AA of Sig Pep	First AA of Secreted Portion	Last AA of ORF
1	HLHDS67	97979 03/27/97	Uni-ZAP XR	11	2526	427	2526	458	458	249	1	30	31	30
2	HLHDZ58	97979 03/27/97	Uni-ZAP XR	12	1131	1	1131	129	129	250	1	14	15	115
3	HLMMJ13	97979 03/27/97	Lambda ZAP II	13	941	39	941	62	62	251	1	44	45	102
3	HLMMJ13	97979 03/27/97	Lambda ZAP II	218	941	39	941	245	245	456	1	35	36	41
4	HLTEI25	97979 03/27/97	Uni-ZAP XR	14	843	1	843	155	155	252	1	19	20	42
5	HMSJX24	97979 03/27/97	Uni-ZAP XR	15	1018	1	1018	90	90	253	1	18	19	36
6	HNFED65	97979 03/27/97	Uni-ZAP XR	16	661	1	661	76	76	254	1	28	29	127
7	HNHDX07	97979 03/27/97	Uni-ZAP XR	17	553	1	553	106	106	255	1	23	24	66
8	HNHGC82	97979 03/27/97	Uni-ZAP XR	18	869	1	869	101	101	256	1	21	22	68

Gene No.	cDNA Clone ID	ATCC Deposit No:Z and Date	Vector	NT SEQ ID NO: X	Total NT Seq.	5' NT of Clone Seq.	3' NT of Clone Seq.	5' NT of Start Codon	5' NT of First AA of Signal Pep	AA SEQ ID NO: Y	First AA of Sig Pep	Last AA of Sig Pep	First AA of Secreted Portion	Last AA of ORF
9	HNHGO09	97979 03/27/97	Uni-ZAP XR	19	959	1	959	176	176	257	1	21	22	43
10	HOUBE18	97979 03/27/97	Uni-ZAP XR	20	1446	1	1446	101	101	258	1	27	28	50
11	HOUDL69	97979 03/27/97	Uni-ZAP XR	21	1471	579	1460	692	692	259	1	31	32	42
12	HPMFI71	97979 03/27/97	Uni-ZAP XR	22	1402	242	1402	401	401	260	1	32	33	60
13	HPMGQ55	97979 03/27/97	Uni-ZAP XR	23	1047	1	1047	164	164	261	1	26	27	35
14	HPQAC69	97979 03/27/97	Lambda ZAP II	24	990	1	988	82	82	262	1	20	21	37
15	HPTBB03	97979 03/27/97	Uni-ZAP XR	25	1208	350	1173	398	398	263	1	29	30	210
16	HPTWA66	97979 03/27/97	pBluescript	26	1922	1381	1922	24	24	264	1	33	34	547
16	HPTWA66	97979 03/27/97	pBluescript	219	575	1	575	148	148	457	1	22	23	65
17	HPTWC08	97979 03/27/97	pBluescript	27	1951	1422	1874	219	219	265	1	19	20	299
18	HRGCZ46	97979 03/27/97	Uni-ZAP XR	28	3989	2635	3989		2748	266	1	16	17	39

Gene No.	cDNA Clone ID	ATCC Deposit No:Z and Date	Vector	NT SEQ ID NO: X	Total NT Seq.	5' NT of Clone Seq.	3' NT of Clone Seq.	5' NT of Start Codon	5' NT of First AA of Signal Pep	AA SEQ ID NO: Y	First AA of Sig Pep	Last AA of Sig Pep	First AA of Secreted Portion	Last AA of ORF
19	HSAVU34	97979 03/27/97	Uni-ZAP XR	29	3735	2966	3735	272	272	267	1	30	31	594
19	HSAVU34	97979 03/27/97	Uni-ZAP XR	220	3018	1929	3018	26	26	458	1	1	2	156
20	HSDFW61	97974 04/04/97 209080 05/29/97	Uni-ZAP XR	30	1667	59	1625	138	138	268	1	32	33	130
21	HSDGP60	97974 04/04/97 209080 05/29/97	Uni-ZAP XR	31	1408	1	1408	285	285	269	1			20
22	HSOAJ55	97974 04/04/97 209080 05/29/97	Uni-ZAP XR	32	3186	2402	3186	302	302	270	1	43	44	159
22	HSOAJ55	97974 04/04/97 209080 05/29/97	Uni-ZAP XR	221	2031	1273	2031	1285	1285	459	1	29	30	30

Gene No.	cDNA Clone ID	ATCC Deposit No:Z and Date	Vector	NT SEQ ID NO: X	Total NT Seq.	5' NT of Clone Seq.	3' NT of Clone Seq.	5' NT of Start Codon	5' NT of First AA of Signal Pep	AA SEQ ID NO: Y	First AA of Sig Pep	Last AA of Sig Pep	First AA of Secreted Portion	Last AA of ORF
23	HSQEO84	97974 04/04/97 209080 05/29/97	Uni-ZAP XR	33	971	13	971	91	91	271	1	19	20	218
23	HSQEO84	97974 04/04/97 209080 05/29/97	Uni-ZAP XR	222	968	8	968	86	86	460	1	20	21	56
24	HSXAM05	97974 04/04/97 209080 05/29/97	Uni-ZAP XR	34	1792	369	1792	470	470	272	1	26	27	49
25	HSXAS67	97974 04/04/97 209080 05/29/97	Uni-ZAP XR	35	896	1	896	96	96	273	1	32	33	121
26	HTDAF28	97974 04/04/97 209080 05/29/97	pSport1	36	912	1	912	38	38	274	1	22	23	87

Gene No.	cDNA Clone ID	ATCC Deposit No:Z and Date	Vector	NT SEQ ID NO: X	Total NT Seq.	5' NT of Clone Seq.	3' NT of Clone Seq.	5' NT of Start Codon	5' NT of First AA of Signal Pep	AA SEQ ID NO: Y	First AA of Sig Pep	Last AA of Sig Pep	First AA of Secreted Portion	Last AA of ORF
27	HTEGQ64	97974 04/04/97 209080 05/29/97	Uni-ZAP XR	37	1382	67	1382	271	271	275	1			25
28	HTGEU09	97974 04/04/97 209080 05/29/97	Uni-ZAP XR	38	872	1	872	74	74	276	1	18	19	28
29	HTOAM21	97974 04/04/97 209080 05/29/97	Uni-ZAP XR	39	812	1	812	41	41	277	1	30	31	43
30	HTPBW79	209511 12/03/97	Uni-ZAP XR	40	1515	118	1507	302	302	278	1	24	25	362
30	HTSEV09	97974 04/04/97 209080 05/29/97	pBluescript	223	1404	1	1265	92	92	461	1	19	20	415
31	HJPCD40	97974 04/04/97 209080 05/29/97	Uni-ZAP XR	41	704	22	704		117	279	1	18	19	127

Gene No.	cDNA Clone ID	ATCC Deposit No:Z and Date	Vector	NT SEQ ID NO: X	Total NT Seq.	5' NT of Clone Seq.	3' NT of Clone Seq.	5' NT of Start Codon	5' NT of First AA of Signal Pep	AA SEQ ID NO: Y	First AA of Sig Pep	Last AA of Sig Pep	First AA of Secreted Portion	Last AA of ORF
32	HTWBY48	97974 04/04/97 209080 05/29/97	pSport1	42	1094	1	1094	32	32	280	1	34	35	53
33	HTWCI46	97974 04/04/97 209080 05/29/97	pSport1	43	1821	892	1647	56	56	281	1	26	27	29
34	HTXGI75	97974 04/04/97 209080 05/29/97	Uni-ZAP XR	44	1024	30	1024		167	282	1	20	21	25
35	HWTBF59	97974 04/04/97 209080 05/29/97	Uni-ZAP XR	45	983	779	983	85	85	283	1	30	31	221
35	HWTBF59	97974 04/04/97 209080 05/29/97	Uni-ZAP XR	224	707	488	707	514	514	462	1	41	42	64

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Gene No.	cDNA Clone ID	ATCC Deposit No:Z and Date	Vector	NT SEQ ID NO: X	Total NT Seq.	5' NT of Clone Seq.	3' NT of Clone Seq.	5' NT of Start Codon	5' NT of First AA of Signal Pep	AA SEQ ID NO: Y	First AA of Sig Pep	Last AA of Sig Pep	First AA of Secreted Portion	Last AA of ORF
36	HADAE74	97974 04/04/97 209080 05/29/97	pSport1	46	2421	664	1587	2110	2110	284	1	33	34	40
37	HAGFB60	97974 04/04/97 209080 05/29/97	Uni-ZAP XR	47	840	1	840	97	97	285	1	30	31	48
38	HATEF60	97974 04/04/97 209080 05/29/97	Uni-ZAP XR	48	2432	1193	2246	1491	1491	286	1	17	18	51
39	HBMSN25	97974 04/04/97 209080 05/29/97	Uni-ZAP XR	49	1742	1165	1742	1207	1207	287	1	23	24	31
40	HCDAR68	97974 04/04/97 209080 05/29/97	Uni-ZAP XR	50	1487	181	1455	325	325	288	1	35	36	56

Gene No.	cDNA Clone ID	ATCC Deposit No:Z and Date	Vector	NT SEQ ID NO: X	Total NT Seq.	5' NT of Clone Seq.	3' NT of Clone Seq.	5' NT of Start Codon	5' NT of First AA of Signal Pep	AA SEQ ID NO: Y	First AA of Sig Pep	Last AA of Sig Pep	First AA of Secreted Portion	Last AA of ORF
41	HCE3J79	97974 04/04/97 209080 05/29/97	Uni-ZAP XR	51	1328	251	1328	525	525	289	1			21
42	HMDAN54	97974 04/04/97 209080 05/29/97	Uni-ZAP XR	52	1856	725	1853	928	928	290	1	33	34	50
43	HCECA49	97974 04/04/97 209080 05/29/97	Uni-ZAP XR	53	1558	310	1408	109	109	291	1	30	31	98
44	HCEEC15	97974 04/04/97 209080 05/29/97	Uni-ZAP XR	54	948	1	948	9	9	292	1	23	24	65
45	HCESF40	97974 04/04/97 209080 05/29/97	pBluescript	55	990	99	990	193	193	293	1	32	33	256

Gene No.	cDNA Clone ID	ATCC Deposit No:Z and Date	Vector	NT SEQ ID NO: X	Total NT Seq.	5' NT of Clone Seq.	3' NT of Clone Seq.	5' NT of Start Codon	5' NT of First AA of Signal Pep	AA SEQ ID NO: Y	First AA of Sig Pep	Last AA of Sig Pep	First AA of Secreted Portion	Last AA of ORF
45	HCESF40	97974 04/04/97 209080 05/29/97	pBluescript	225	1384	99	1384	193	193	463	1	32	33	205
46	HCFMV39	97974 04/04/97 209080 05/29/97	pSport1	56	1603	1	1296	96	96	294	1	29	30	102
47	HCMSX86	97975 04/04/97 209081 05/29/97	Uni-ZAP XR	57	1052	5	786	12	12	295	1	28	29	32
48	HCNAP62	97975 04/04/97 209081 05/29/97	Lambda ZAP II	58	814	1	558	93	93	296	1	22	23	42
49	HCRAF32	97975 04/04/97 209081 05/29/97	Uni-ZAP XR	59	1215	257	1215		356	297	1	19	20	20

Gene No.	cDNA Clone ID	ATCC Deposit No:Z and Date	Vector	NT SEQ ID NO: X	Total NT Seq.	5' NT of Clone Seq.	3' NT of Clone Seq.	5' NT of Start Codon	5' NT of First AA of Signal Pep	AA SEQ ID NO: Y	First AA of Sig Pep	Last AA of Sig Pep	First AA of Secreted Portion	Last AA of ORF
50	HCUDC07	97975 04/04/97 209081 05/29/97	ZAP Express	60	478	1	478	147	147	298	1	36	37	69
51	HCWBB42	97975 04/04/97 209081 05/29/97	ZAP Express	61	618	1	618	212	212	299	1	35	36	74
52	HDTAB05	97975 04/04/97 209081 05/29/97	pCMVSport 2.0	62	751	1	751	257	257	300	1	21	22	32
53	HE2AV74	97975 04/04/97 209081 05/29/97	Uni-ZAP XR	63	780	283	780		433	301	1			16
54	HE2AY71	97975 04/04/97 209081 05/29/97	Uni-ZAP XR	64	588	21	588	169	169	302	1			16

Gene No.	cDNA Clone ID	ATCC Deposit No:Z and Date	Vector	NT SEQ ID NO: X	Total NT Seq.	5' NT of Clone Seq.	3' NT of Clone Seq.	5' NT of Start Codon	5' NT of First AA of Signal Pep	AA SEQ ID NO: Y	First AA of Sig Pep	Last AA of Sig Pep	First AA of Secreted Portion	Last AA of ORF
55	HE2GS36	97975 04/04/97 209081 05/29/97	Uni-ZAP XR	65	945	1	349	520	520	303	1	39	40	111
55	HE2GS36	97975 04/04/97 209081 05/29/97	Uni-ZAP XR	226	774	272	774	445	445	464	1			37
56	HE2OF09	97975 04/04/97 209081 05/29/97	Uni-ZAP XR	66	1866	1313	1866	1596	1596	304	1			11
57	HE6EU50	97975 04/04/97 209081 05/29/97	Uni-ZAP XR	67	1152	117	686	237	237	305	1	20	21	34
58	HE9HU17	97975 04/04/97 209081 05/29/97	Uni-ZAP XR	68	2483	1577	2448	1620	1620	306	1			14

Gene No.	cDNA Clone ID	ATCC Deposit No:Z and Date	Vector	NT SEQ ID NO: X	Total NT Seq.	5' NT of Clone Seq.	3' NT of Clone Seq.	5' NT of Start Codon	5' NT of First AA of Signal Pep	AA SEQ ID NO: Y	First AA of Sig Pep	Last AA of Sig Pep	First AA of Secreted Portion	Last AA of ORF
59	HE9ND48	97975 04/04/97 209081 05/29/97	Uni-ZAP XR	69	536	1	536	83	83	307	1	36	37	43
60	HEBBW11	97975 04/04/97 209081 05/29/97	Uni-ZAP XR	70	574	97	564	109	109	308	1	55	56	137
60	HEBBW11	97975 04/04/97 209081 05/29/97	Uni-ZAP XR	227	865	647	865		388	465	1	30	31	135
61	HELDY74	97975 04/04/97 209081 05/29/97	Uni-ZAP XR	71	932	1	932	201	201	309	1	17	18	33
62	HEMAE80	97975 04/04/97 209081 05/29/97	Uni-ZAP XR	72	996	1	945	12	12	310	1	24	25	136

Gene No.	cDNA Clone ID	ATCC Deposit No:Z and Date	Vector	NT SEQ ID NO: X	Total NT Seq.	5' NT of Clone Seq.	3' NT of Clone Seq.	5' NT of Start Codon	5' NT of First AA of Signal Pep	AA SEQ ID NO: Y	First AA of Sig Pep	Last AA of Sig Pep	First AA of Secreted Portion	Last AA of ORF
63	HFEBA88	97975 04/04/97 209081 05/29/97	Uni-ZAP XR	73	785	464	785	356	356	311	1	29	30	57
64	HFGAB89	97975 04/04/97 209081 05/29/97	Uni-ZAP XR	74	1069	196	1047	295	295	312	1	32	33	34
65	HFVHY45	97975 04/04/97 209081 05/29/97	pBluescript	75	831	1	831	50	50	313	1	36	37	89
66	HGBAJ93	97975 04/04/97 209081 05/29/97	Uni-ZAP XR	76	590	1	590	233	233	314	1	38	39	94
67	HGBBQ69	97975 04/04/97 209081 05/29/97	Uni-ZAP XR	77	1274	1	1273	105	105	315	1	24	25	43

Gene No.	cDNA Clone ID	ATCC Deposit No:Z and Date	Vector	NT SEQ ID NO: X	Total NT Seq.	5' NT of Clone Seq.	3' NT of Clone Seq.	5' NT of Start Codon	5' NT of First AA of Signal Pep	AA SEQ ID NO: Y	First AA of Sig Pep	Last AA of Sig Pep	First AA of Secreted Portion	Last AA of ORF
68	HHFCF08	97975 04/04/97 209081 05/29/97	Uni-ZAP XR	78	1133	4	1042	175	175	316	1	23	24	30
69	HHFHJ59	97975 04/04/97 209081 05/29/97	Uni-ZAP XR	79	661	1	661	192	192	317	1	29	30	112
70	HHFHR32	97975 04/04/97 209081 05/29/97	Uni-ZAP XR	80	1378	1	1378	58	58	318	1	25	26	235
71	HHGCN69	97975 04/04/97 209081 05/29/97	Lambda ZAP II	81	1440	298	1440	532	532	319	1	23	24	34
72	HHGDO13	97975 04/04/97 209081 05/29/97	Lambda ZAP II	82	1381	766	1371	993	993	320	1	23	24	34

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Gene No.	cDNA Clone ID	ATCC Deposit No:Z and Date	Vector	NT SEQ ID NO: X	Total NT Seq.	5' NT of Clone Seq.	3' NT of Clone Seq.	5' NT of Start Codon	5' NT of First AA of Signal Pep	AA SEQ ID NO: Y	First AA of Sig Pep	Last AA of Sig Pep	First AA of Secreted Portion	Last AA of ORF
73	HHPFD63	97975 04/04/97 209081 05/29/97	Uni-ZAP XR	83	1706	182	1644	257	257	321	1	24	25	81
74	HHSEG23	97976 04/04/97	Uni-ZAP XR	84	573	1	573	160	160	322	1	18	19	71
75	HJPAV06	97976 04/04/97	Uni-ZAP XR	85	684	199	684	323	323	323	1	27	28	33
76	HKIXL73	97976 04/04/97	pBluescript	86	1036	591	1036	690	690	324	1	32	33	114
77	HKMNC43	97976 04/04/97	pBluescript	87	908	1	908	139	139	325	1	18	19	108
78	HMEJE31	97976 04/04/97	Lambda ZAP II	88	655	1	655	165	165	326	1	33	34	64
79	HMSKS35	97976 04/04/97	Uni-ZAP XR	89	1102	1	1102	228	228	327	1	23	24	49
79	HMSKS35	97976 04/04/97	Uni-ZAP XR	228	1102	1	1102	228	228	466	1	26	27	49
80	HNFAE54	97976 04/04/97	Uni-ZAP XR	90	1533	665	1518	347	347	328	1	26	27	293
81	HNFJH45	97976 04/04/97	Uni-ZAP XR	91	575	1	575	275	275	329	1	30	31	67

Gene No.	cDNA Clone ID	ATCC Deposit No:Z and Date	Vector	NT SEQ ID NO: X	Total NT Seq.	5' NT of Clone Seq.	3' NT of Clone Seq.	5' NT of Start Codon	5' NT of First AA of Signal Pep	AA SEQ ID NO: Y	First AA of Sig Pep	Last AA of Sig Pep	First AA of Secreted Portion	Last AA of ORF
82	HNGBT31	97976 04/04/97	Uni-ZAP XR	92	639	1	639	224	224	330	1	28	29	104
83	HNGIN60	97976 04/04/97	Uni-ZAP XR	93	858	1	858	239	239	331	1	23	24	58
83	HNGIN60	97976 04/04/97	Uni-ZAP XR	229	744	1	744	225	225	467	1	43	44	70
84	HNGJG84	97976 04/04/97	Uni-ZAP XR	94	526	1	526	268	268	332	1	29	30	38
85	HNHDW42	97976 04/04/97	Uni-ZAP XR	95	426	1	426	168	168	333	1	28	29	71
86	HNHFL57	97976 04/04/97	Uni-ZAP XR	96	844	1	844	98	98	334	1	25	26	61
87	HOGAR52	97977 04/04/97 209082 05/29/97	pCMVSport 2.0	97	1985	453	1985	533	533	335	1	17	18	285
88	HOSBZ55	97977 04/04/97 209082 05/29/97	Uni-ZAP XR	98	1416	69	1416	246	246	336	1	32	33	54

Gene No.	cDNA Clone ID	ATCC Deposit No:Z and Date	Vector	NT SEQ ID NO: X	Total NT Seq.	5' NT of Clone Seq.	3' NT of Clone Seq.	5' NT of Start Codon	5' NT of First AA of Signal Pep	AA SEQ ID NO: Y	First AA of Sig Pep	Last AA of Sig Pep	First AA of Secreted Portion	Last AA of ORF
89	HOSDI92	97977 04/04/97 209082 05/29/97	Uni-ZAP XR	99	1760	1469	1760	934	934	337	1	22	23	59
89	HOSDI92	97977 04/04/97 209082 05/29/97	Uni-ZAP XR	230	1935	141	772		274	468	1	20	21	58
90	HPBCU51	97977 04/04/97 209082 05/29/97	pBluescript SK-	100	599	1	599	86	86	338	1	27	28	119
91	HPCAL49	97977 04/04/97 209082 05/29/97	Uni-ZAP XR	101	784	1	784	113	113	339	1	36	37	38
92	HPFCR13	97977 04/04/97 209082 05/29/97	Uni-ZAP XR	102	404	1	404	266	266	340	1	30	31	46

Gene No.	cDNA Clone ID	ATCC Deposit No:Z and Date	Vector	NT SEQ ID NO: X	Total NT Seq.	5' NT of Clone Seq.	3' NT of Clone Seq.	5' NT of Start Codon	5' NT of First AA of Signal Pep	AA SEQ ID NO: Y	First AA of Sig Pep	Last AA of Sig Pep	First AA of Secreted Portion	Last AA of ORF
92	HPFCR13	97977 04/04/97 209082 05/29/97	Uni-ZAP XR	231	1035	602	1035	859	859	469	1	32	33	58
93	HPHAC83	97977 04/04/97 209082 05/29/97	Uni-ZAP XR	103	2218	840	2182	1035	1035	341	1	17	18	17
93	HOFNZ45	209568 01/06/98	pCMVSport 2.0	232	760	1	728	86	86	470	1	36	37	61
94	HPMBQ32	97977 04/04/97 209082 05/29/97	Uni-ZAP XR	104	1351	1	1351	18	18	342	1	23	24	86
95	HPWAN23	97977 04/04/97 209082 05/29/97	Uni-ZAP XR	105	2066	51	2052	270	270	343	1	29	30	537
95	HPWAN23	97977 04/04/97 209082 05/29/97	Uni-ZAP XR	233	2057	1	1954	220	220	471	1	29	30	315

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Gene No.	cDNA Clone ID	ATCC Deposit No:Z and Date	Vector	NT SEQ ID NO: X	Total NT Seq.	5' NT of Clone Seq.	3' NT of Clone Seq.	5' NT of Start Codon	5' NT of First AA of Signal Pep	AA SEQ ID NO: Y	First AA of Sig Pep	Last AA of Sig Pep	First AA of Secreted Portion	Last AA of ORF
96	HRDFB85	97977 04/04/97 209082 05/29/97	Uni-ZAP XR	106	1705	23	1697	233	233	344	1	21	22	201
97	HRGBR28	97977 04/04/97 209082 05/29/97	Uni-ZAP XR	107	1167	1	557	604	604	345	1	22	23	122
98	HSKGN81	97977 04/04/97 209082 05/29/97	pBluescript	108	1907	151	1432	353	353	346	1	23	24	260
98	HSKGN81	97977 04/04/97 209082 05/29/97	pBluescript	234	2084	335	2084	537	537	472	1	19	20	23
99	HSPAH56	97977 04/04/97 209082 05/29/97	pSport1	109	611	1	576	229	229	347	1	25	26	47
100	HE8EU04	209746 04/07/98	Uni-ZAP XR	110	2632	294	2632	337	337	348	1	25	26	333

Gene No.	cDNA Clone ID	ATCC Deposit No:Z and Date	Vector	NT SEQ ID NO: X	Total NT Seq.	5' NT of Clone Seq.	3' NT of Clone Seq.	5' NT of Start Codon	5' NT of First AA of Signal Pep	AA SEQ ID NO: Y	First AA of Sig Pep	Last AA of Sig Pep	First AA of Secreted Portion	Last AA of ORF
100	HSXBT86	97977 04/04/97 209082 05/29/97	Uni-ZAP XR	235	2143	53	1096	235	235	473	1			9
101	HSXCS62	97977 04/04/97 209082 05/29/97	Uni-ZAP XR	111	2249	1	1953	90	90	349	1	18	19	199
102	HTEFU09	97977 04/04/97 209082 05/29/97	Uni-ZAP XR	112	2198	228	2158	400	400	350	1			23
103	HTEKM35	97977 04/04/97 209082 05/29/97	Uni-ZAP XR	113	1043	40	1043	320	320	351	1	20	21	142
104	HTGEP89	97977 04/04/97 209082 05/29/97	Uni-ZAP XR	114	703	1	703	285	285	352	1	29	30	94

Gene No.	cDNA Clone ID	ATCC Deposit No:Z and Date	Vector	NT SEQ ID NO: X	Total NT Seq.	5' NT of Clone Seq.	3' NT of Clone Seq.	5' NT of Start Codon	5' NT of First AA of Signal Pep	AA SEQ ID NO: Y	First AA of Sig Pep	Last AA of Sig Pep	First AA of Secreted Portion	Last AA of ORF
105	HTGEW91	97977 04/04/97 209082 05/29/97	Uni-ZAP XR	115	3684	526	1338	584	584	353	1	24	25	37
106	HTOEY16	97977 04/04/97 209082 05/29/97	Uni-ZAP XR	116	1965	127	1915	202	202	354	1	27	28	38
107	HTPCN79	97977 04/04/97 209082 05/29/97	Uni-ZAP XR	117	503	1	503		1	355	1	7	8	70
108	HTSGM54	97977 04/04/97 209082 05/29/97	pBluescript	118	1071	50	981	29	29	356	1	30	31	227
108	HTSGM54	97977 04/04/97 209082 05/29/97	pBluescript	236	1133	316	1069		423	474	1	12	13	84

Gene No.	cDNA Clone ID	ATCC Deposit No:Z and Date	Vector	NT SEQ ID NO: X	Total NT Seq.	5' NT of Clone Seq.	3' NT of Clone Seq.	5' NT of Start Codon	5' NT of First AA of Signal Pep	AA SEQ ID NO: Y	First AA of Sig Pep	Last AA of Sig Pep	First AA of Secreted Portion	Last AA of ORF
109	HTSHE40	97977 04/04/97 209082 05/29/97	pBluescript	119	1101	118	956	218	218	357	1	31	32	89
110	HTWAF58	97977 04/04/97 209082 05/29/97	Lambda ZAP II	120	282	1	282	137	137	358	1	25	26	48
111	HTWBY29	97977 04/04/97 209082 05/29/97	pSport1	121	2635	1593	2489	1654	1654	359	1	25	26	55
112	HUKFC71	209007 04/28/97 209083 05/29/97	Lambda ZAP II	122	994	1	932		272	360	1	15	16	221
113	HCE3Q10	209007 04/28/97 209083 05/29/97	Uni-ZAP XR	123	1542	1	1542	143	143	361	1	25	26	63

Gene No.	cDNA Clone ID	ATCC Deposit No:Z and Date	Vector	NT SEQ ID NO: X	Total NT Seq.	5' NT of Clone Seq.	3' NT of Clone Seq.	5' NT of Start Codon	5' NT of First AA of Signal Pep	AA SEQ ID NO: Y	First AA of Sig Pep	Last AA of Sig Pep	First AA of Secreted Portion	Last AA of ORF
114	HCEVR60	209007 04/28/97 209083 05/29/97	Uni-ZAP XR	124	1390	82	1390	127	127	362	1	32	33	153
115	HDTAW95	209007 04/28/97 209083 05/29/97	pCMVSport 2.0	125	1288	412	1288	571	571	363	1			16
116	HE6EL90	209007 04/28/97 209083 05/29/97	Uni-ZAP XR	126	1517	1	1452	243	243	364	1			9
117	HELBU29	209007 04/28/97 209083 05/29/97	Uni-ZAP XR	127	1073	198	1073		776	365	1			13
118	HERAH36	209007 04/28/97 209083 05/29/97	Uni-ZAP XR	128	300	155	300	202	202	366	1			17

Gene No.	cDNA Clone ID	ATCC Deposit No:Z and Date	Vector	NT SEQ ID NO: X	Total NT Seq.	5' NT of Clone Seq.	3' NT of Clone Seq.	5' NT of Start Codon	5' NT of First AA of Signal Pep	AA SEQ ID NO: Y	First AA of Sig Pep	Last AA of Sig Pep	First AA of Secreted Portion	Last AA of ORF
119	HFXBW82	209007 04/28/97 209083 05/29/97	Lambda ZAP II	129	1275	1	1275	56	56	367	1	23	24	61
120	HHPTD20	209007 04/28/97 209083 05/29/97	Uni-ZAP XR	130	472	51	472		243	368	1			32
121	HIBED17	209007 04/28/97 209083 05/29/97	Other	131	1950	284	1927	395	395	369	1	72	73	245
122	HLTER03	209007 04/28/97 209083 05/29/97	Uni-ZAP XR	132	990	1	990	78	78	370	1	22	23	34
123	HOABL56	209007 04/28/97 209083 05/29/97	Uni-ZAP XR	133	1720	565	1720	660	660	371	1	18	19	21

Gene No.	cDNA Clone ID	ATCC Deposit No:Z and Date	Vector	NT SEQ ID NO: X	Total NT Seq.	5' NT of Clone Seq.	3' NT of Clone Seq.	5' NT of Start Codon	5' NT of First AA of Signal Pep	AA SEQ ID NO: Y	First AA of Sig Pep	Last AA of Sig Pep	First AA of Secreted Portion	Last AA of ORF
124	HPMCJ92	209007 04/28/97 209083 05/29/97	Uni-ZAP XR	134	705	28	705	106	106	372	1	28	29	98
125	HPWAZ95	209007 04/28/97 209083 05/29/97	Uni-ZAP XR	135	323	1	323	88	88	373	1	27	28	78
126	HRGBR18	209007 04/28/97 209083 05/29/97	Uni-ZAP XR	136	582	1	582		16	374	1	17	18	30
127	HSUBW09	209007 04/28/97 209083 05/29/97	Uni-ZAP XR	137	1021	1	1021	153	153	375	1	32	33	56
128	HUKCO64	209007 04/28/97 209083 05/29/97	Lambda ZAP II	138	1777	1	1339	198	198	376	1	23	24	63

TO2280" Z9ZEE660

Gene No.	cDNA Clone ID	ATCC Deposit No:Z and Date	Vector	NT SEQ ID NO: X	Total NT Seq.	5' NT of Clone Seq.	3' NT of Clone Seq.	5' NT of Start Codon	5' NT of First AA of Signal Pep	AA SEQ ID NO: Y	First AA of Sig Pep	Last AA of Sig Pep	First AA of Secreted Portion	Last AA of ORF
129	H6EAA53	209007 04/28/97 209083 05/29/97	Uni-ZAP XR	139	643	303	643	306	306	377	1	14	15	38
130	HAGAI11	209007 04/28/97 209083 05/29/97	Uni-ZAP XR	140	1220	1	1220	567	567	378	1	50	51	98
131	HAGAO39	209007 04/28/97 209083 05/29/97	Uni-ZAP XR	141	721	1	721		415	379	1			14
132	HALSK07	209007 04/28/97 209083 05/29/97	Uni-ZAP XR	142	1468	125	1468	210	210	380	1	29	30	33
133	HALSQ59	209007 04/28/97 209083 05/29/97	Uni-ZAP XR	143	300	4	300	101	101	381	1	22	23	66
134	HAIBP89	209877 05/18/98	Uni-ZAP XR	144	2243	173	2243	311	311	382	1	27	28	317

Gene No.	cDNA Clone ID	ATCC Deposit No:Z and Date	Vector	NT SEQ ID NO: X	Total NT Seq.	5' NT of Clone Seq.	3' NT of Clone Seq.	5' NT of Start Codon	5' NT of First AA of Signal Pep	AA SEQ ID NO: Y	First AA of Sig Pep	Last AA of Sig Pep	First AA of Secreted Portion	Last AA of ORF
134	HBGCB91	209007 04/28/97 209083 05/29/97	Uni-ZAP XR	237	1025	409	1025	624	624	475	1	20	21	25
135	HBMTD81	209008 04/28/97 209084 05/29/97	Uni-ZAP XR	145	1082	163	1082	357	357	383	1			30
136	HBXGK12	209008 04/28/97 209084 05/29/97	ZAP Express	146	4313	1153	4313	1313	1313	384	1	18	19	42
137	HFKFJ07	209010 04/28/97 209085 05/29/97	Uni-ZAP XR	147	1183	1	1183	149	149	385	1	41	42	254
138	HCQAI40	209008 04/28/97 209084 05/29/97	Lambda ZAP II	148	734	1	734	285	285	386	1			19

Gene No.	cDNA Clone ID	ATCC Deposit No:Z and Date	Vector	NT SEQ ID NO: X	Total NT Seq.	5' NT of Clone Seq.	3' NT of Clone Seq.	5' NT of Start Codon	5' NT of First AA of Signal Pep	AA SEQ ID NO: Y	First AA of Sig Pep	Last AA of Sig Pep	First AA of Secreted Portion	Last AA of ORF
139	HCWHZ24	209008 04/28/97 209084 05/29/97	ZAP Express	149	1405	1	1405	108	108	387	1	34	35	63
140	HE2GT20	209008 04/28/97 209084 05/29/97	Uni-ZAP XR	150	2890	1178	2890	1178	1178	388	1	31	32	39
141	HE8EY43	209008 04/28/97 209084 05/29/97	Uni-ZAP XR	151	2399	1181	2399	1265	1265	389	1	30	31	34
142	HFCEB37	209008 04/28/97 209084 05/29/97	Uni-ZAP XR	152	802	352	802		487	390	1			10
143	HFTCT67	209008 04/28/97 209084 05/29/97	Uni-ZAP XR	153	461	24	461	145	145	391	1	37	38	63

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Gene No.	cDNA Clone ID	ATCC Deposit No:Z and Date	Vector	NT SEQ ID NO: X	Total NT Seq.	5' NT of Clone Seq.	3' NT of Clone Seq.	5' NT of Start Codon	5' NT of First AA of Signal Pep	AA SEQ ID NO: Y	First AA of Sig Pep	Last AA of Sig Pep	First AA of Secreted Portion	Last AA of ORF
144	HGLAM46	209008 04/28/97 209084 05/29/97	Uni-ZAP XR	154	2388	818	2388	648	648	392	1			18
145	HHGBR15	209008 04/28/97 209084 05/29/97	Lambda ZAP II	155	642	322	642	369	369	393	1	41	42	43
146	HJAAU36	209008 04/28/97 209084 05/29/97	pBluescript SK-	156	1251	583	1251		933	394	1	16	17	16
147	HUSIT49	209008 04/28/97 209084 05/29/97	pSport1	157	2127	247	2127	383	383	395	1	47	48	83
148	HKLAB16	209008 04/28/97 209084 05/29/97	Lambda ZAP II	158	1625	817	1625	1012	1012	396	1	18	19	20

Gene No.	cDNA Clone ID	ATCC Deposit No:Z and Date	Vector	NT SEQ ID NO: X	Total NT Seq.	5' NT of Clone Seq.	3' NT of Clone Seq.	5' NT of Start Codon	5' NT of First AA of Signal Pep	AA SEQ ID NO: Y	First AA of Sig Pep	Last AA of Sig Pep	First AA of Secreted Portion	Last AA of ORF
149	HLMMU76	209008 04/28/97 209084 05/29/97	Lambda ZAP II	159	1687	1307	1687	1296	1296	397	1	28	29	28
150	HMSKQ35	209008 04/28/97 209084 05/29/97	Uni-ZAP XR	160	1842	172	1463	319	319	398	1	30	31	33
151	HNHED86	209008 04/28/97 209084 05/29/97	Uni-ZAP XR	161	770	1	770	30	30	399	1	31	32	46
152	HNHEJ88	209008 04/28/97 209084 05/29/97	Uni-ZAP XR	162	519	1	519	242	242	400	1	17	18	24
153	HNHFQ63	209008 04/28/97 209084 05/29/97	Uni-ZAP XR	163	753	1	753	164	164	401	1	17	18	67
154	HOECU83	209009 04/28/97	Uni-ZAP XR	164	1893	1	1211	1637	1637	402	1	28	29	85

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Gene No.	cDNA Clone ID	ATCC Deposit No:Z and Date	Vector	NT SEQ ID NO: X	Total NT Seq.	5' NT of Clone Seq.	3' NT of Clone Seq.	5' NT of Start Codon	5' NT of First AA of Signal Pep	AA SEQ ID NO: Y	First AA of Sig Pep	Last AA of Sig Pep	First AA of Secreted Portion	Last AA of ORF
154	HOECU83	209009 04/28/97	Uni-ZAP XR	238	1400	189	1400		508	476	1	22	23	33
155	HPTRC15	209009 04/28/97	pBluescript	165	2153	594	2153	57	57	403	1	26	27	82
156	HSKCP69	209009 04/28/97	Uni-ZAP XR	166	1251	219	1120	49	49	404	1	27	28	286
156	HSKCP69	209009 04/28/97	Uni-ZAP XR	239	1250	223	1250	393	393	477	1	32	33	171
157	H6EAE26	209009 04/28/97	Uni-ZAP XR	167	882	48	882	155	155	405	1	33	34	153
158	HAGBX03	209009 04/28/97	Uni-ZAP XR	168	1208	1	1208	290	290	406	1	20	21	37
159	HAGDQ47	209009 04/28/97	Uni-ZAP XR	169	1258	1	1258	44	44	407	1	22	23	60
159	HAGDQ47	209009 04/28/97	Uni-ZAP XR	240	1307	1	1307	44	44	478	1	22	23	60
160	HAICP19	209009 04/28/97	Uni-ZAP XR	170	1624	89	1483	128	128	408	1	18	19	446
161	HAUAE83	209009 04/28/97	Uni-ZAP XR	171	2003	889	2003	957	957	409	1	29	30	64
162	HBHAD12	209009 04/28/97	Uni-ZAP XR	172	786	1	786		176	410	1	17	18	23

Gene No.	cDNA Clone ID	ATCC Deposit No:Z and Date	Vector	NT SEQ ID NO: X	Total NT Seq.	5' NT of Clone Seq.	3' NT of Clone Seq.	5' NT of Start Codon	5' NT of First AA of Signal Pep	AA SEQ ID NO: Y	First AA of Sig Pep	Last AA of Sig Pep	First AA of Secreted Portion	Last AA of ORF
163	HBMTY28	209009 04/28/97	Uni-ZAP XR	173	1758	962	1758	1184	1184	411	1	27	28	34
164	HBMVP04	209009 04/28/97	Uni-ZAP XR	174	1369	29	557	947	947	412	1	33	34	41
164	HBMVP04	209009 04/28/97	Uni-ZAP XR	241	888	330	862		546	479	1			2
165	HCDDB78	209009 04/28/97	Uni-ZAP XR	175	2379	750	2379	901	901	413	1	18	19	24
166	HCEQA68	209010 04/28/97 209085 05/29/97	Uni-ZAP XR	176	1348	1	1348	12	12	414	1	28	29	78
167	HCEZS40	209010 04/28/97 209085 05/29/97	Uni-ZAP XR	177	1502	178	1502	388	388	415	1	31	32	51
168	HCFNF11	209010 04/28/97 209085 05/29/97	pSport1	178	1637	26	1607	152	152	416	1	44	45	257

Gene No.	cDNA Clone ID	ATCC Deposit No:Z and Date	Vector	NT SEQ ID NO: X	Total NT Seq.	5' NT of Clone Seq.	3' NT of Clone Seq.	5' NT of Start Codon	5' NT of First AA of Signal Pep	AA SEQ ID NO: Y	First AA of Sig Pep	Last AA of Sig Pep	First AA of Secreted Portion	Last AA of ORF
169	HCRBL20	209010 04/28/97 209085 05/29/97	Uni-ZAP XR	179	2911	1103	2858	192	192	417	1	32	33	424
169	HCRBL20	209010 04/28/97 209085 05/29/97	Uni-ZAP XR	242	1811	20	1811	93	93	480	1	36	37	95
170	HCUBL62	209010 04/28/97 209085 05/29/97	ZAP Express	180	519	1	519	57	57	418	1	28	29	32
171	HDSAP81	209010 04/28/97 209085 05/29/97	Uni-ZAP XR	181	968	320	968	476	476	419	1	27	28	79
172	HE2CT29	209010 04/28/97 209085 05/29/97	Uni-ZAP XR	182	1128	1	1128	111	111	420	1	26	27	94

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Gene No.	cDNA Clone ID	ATCC Deposit No:Z and Date	Vector	NT SEQ ID NO: X	Total NT Seq.	5' NT of Clone Seq.	3' NT of Clone Seq.	5' NT of Start Codon	5' NT of First AA of Signal Pep	AA SEQ ID NO: Y	First AA of Sig Pep	Last AA of Sig Pep	First AA of Secreted Portion	Last AA of ORF
173	HE8MG65	209010 04/28/97 209085 05/29/97	Uni-ZAP XR	183	2276	48	2276	88	88	421	1	37	38	257
173	HE8MG65	209010 04/28/97 209085 05/29/97	Uni-ZAP XR	243	2271	56	2232	79	79	481	1	43	44	170
174	HE9FB42	209010 04/28/97 209085 05/29/97	Uni-ZAP XR	184	3374	86	1705	277	277	422	1	40	41	704
174	HE9FB42	209010 04/28/97 209085 05/29/97	Uni-ZAP XR	244	2500	76	1693	518	518	482	1	1	2	623
175	HEMAM41	209010 04/28/97 209085 05/29/97	Uni-ZAP XR	185	1337	60	1328	175	175	423	1	39	40	190

Gene No.	cDNA Clone ID	ATCC Deposit No:Z and Date	Vector	NT SEQ ID NO: X	Total NT Seq.	5' NT of Clone Seq.	3' NT of Clone Seq.	5' NT of Start Codon	5' NT of First AA of Signal Pep	AA SEQ ID NO: Y	First AA of Sig Pep	Last AA of Sig Pep	First AA of Secreted Portion	Last AA of ORF
175	HEMAM41	209010 04/28/97 209085 05/29/97	Uni-ZAP XR	245	1338	33	1327	175	175	483	1	32	33	91
176	HEMCV19	209010 04/28/97 209085 05/29/97	Uni-ZAP XR	186	941	33	931	79	79	424	1	23	24	178
177	HEMDX17	209010 04/28/97 209085 05/29/97	Uni-ZAP XR	187	678	1	678	131	131	425	1	21	22	40
177	HEMDX17	209010 04/28/97 209085 05/29/97	Uni-ZAP XR	246	654	1	654	137	137	484	1			12
178	HETAR54	209010 04/28/97 209085 05/29/97	Uni-ZAP XR	188	1848	454	1848	948	948	426	1	14	15	232

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Gene No.	cDNA Clone ID	ATCC Deposit No:Z and Date	Vector	NT SEQ ID NO: X	Total NT Seq.	5' NT of Clone Seq.	3' NT of Clone Seq.	5' NT of Start Codon	5' NT of First AA of Signal Pep	AA SEQ ID NO: Y	First AA of Sig Pep	Last AA of Sig Pep	First AA of Secreted Portion	Last AA of ORF
179	HETBX14	209010 04/28/97 209085 05/29/97	Uni-ZAP XR	189	1292	303	1292	207	207	427	1	18	19	250
179	HETBX14	209010 04/28/97 209085 05/29/97	Uni-ZAP XR	247	1146	157	1146		74	485	1	14	15	53
180	HFGAB48	209010 04/28/97 209085 05/29/97	Uni-ZAP XR	190	906	156	906	628	628	428	1	23	24	58
181	HFKFI40	209010 04/28/97 209085 05/29/97	Uni-ZAP XR	191	1941	120	1002	213	213	429	1	18	19	218
182	HFXHN68	209010 04/28/97 209085 05/29/97	Lambda ZAP II	192	2118	777	2118	966	966	430	1	23	24	50
183	HGBFO79	209011 04/28/97	Uni-ZAP XR	193	1538	259	1538	273	273	431	1	23	24	49

Gene No.	cDNA Clone ID	ATCC Deposit No:Z and Date	Vector	NT SEQ ID NO: X	Total NT Seq.	5' NT of Clone Seq.	3' NT of Clone Seq.	5' NT of Start Codon	5' NT of First AA of Signal Pep	AA SEQ ID NO: Y	First AA of Sig Pep	Last AA of Sig Pep	First AA of Secreted Portion	Last AA of ORF
184	HGLAM56	209011 04/28/97	Uni-ZAP XR	194	1098	68	1098		185	432	1	28	29	69
185	HHLBA89	209011 04/28/97	pBluescript SK-	195	1001	1	1001	324	324	433	1	25	26	39
186	HHPDW05	209011 04/28/97	Uni-ZAP XR	196	1458	1	1458	254	254	434	1	17	18	104
186	HHPDW05	209011 04/28/97	Uni-ZAP XR	248	1443	1	1443	246	246	486	1	21	22	21
187	HHPSD37	209011 04/28/97	pBluescript	197	1282	66	1282	171	171	435	1	19	20	37
188	HHPSF70	209011 04/28/97	pBluescript	198	951	26	951		162	436	1	16	17	34
189	HHSAK25	209011 04/28/97	Uni-ZAP XR	199	1740	1390	1740	1534	1534	437	1	19	20	31
190	HIASB53	209011 04/28/97	pBluescript	200	1707	401	1195	652	652	438	1	26	27	126
191	HJABZ65	209011 04/28/97	pBluescript SK-	201	779	1	779	23	23	439	1	26	27	68
192	HJPBB39	209011 04/28/97	Uni-ZAP XR	202	1617	188	1605	182	182	440	1	28	29	91
193	HLHSK94	209011 04/28/97	pBluescript	203	1974	1	1794	112	112	441	1	26	27	379

Gene No.	cDNA Clone ID	ATCC Deposit No:Z and Date	Vector	NT SEQ ID NO: X	Total NT Seq.	5' NT of Clone Seq.	3' NT of Clone Seq.	5' NT of Start Codon	5' NT of First AA of Signal Pep	AA SEQ ID NO: Y	First AA of Sig Pep	Last AA of Sig Pep	First AA of Secreted Portion	Last AA of ORF
194	HLHTC70	209011 04/28/97	pBluescript	204	1057	229	1057	365	365	442	1	23	24	22
195	HLMIW92	209011 04/28/97	Lambda ZAP II	205	721	1	721	244	244	443	1	25	26	46
196	HLTCY93	209011 04/28/97	Uni-ZAP XR	206	2465	988	2465	387	387	444	1	27	28	214
197	HLTDB65	209011 04/28/97	Uni-ZAP XR	207	1480	1	1480		371	445	1	15	16	143
198	HMSHM43	209011 04/28/97	Uni-ZAP XR	208	872	1	872	35	35	446	1	18	19	36
199	HMSHQ24	209011 04/28/97	Uni-ZAP XR	209	1779	16	1779	148	148	447	1	24	25	36
200	HNFAH08	209011 04/28/97	Uni-ZAP XR	210	2110	592	2110	611	611	448	1	18	19	191
201	HNGAO10	209011 04/28/97	Uni-ZAP XR	211	938	1	938	107	107	449	1	27	28	30
202	HNGBE45	209011 04/28/97	Uni-ZAP XR	212	1551	1	1551	114	114	450	1	21	22	100
203	HNHAZ16	209011 04/28/97	Uni-ZAP XR	213	997	1	997	202	202	451	1	24	25	36
204	HNHCM59	209011 04/28/97	Uni-ZAP XR	214	1496	1	1132		165	452	1	28	29	41

Gene No.	cDNA Clone ID	ATCC Deposit No:Z and Date	Vector	NT SEQ ID NO: X	Total NT Seq.	5' NT of Clone Seq.	3' NT of Clone Seq.	5' NT of Start Codon	5' NT of First AA of Signal Pep	AA SEQ ID NO: Y	First AA of Sig Pep	Last AA of Sig Pep	First AA of Secreted Portion	Last AA of ORF
205	HOSFM22	97977 04/04/97 209082 05/29/97	Uni-ZAP XR	215	1308	501	1308	1081	1081	453	1	46	47	48
206	HPHAC88	97977 04/04/97 209082 05/29/97	Uni-ZAP XR	216	1705	384	1705	549	549	454	1	23	24	24
207	HCDEO95	209007 04/28/97 209083 05/29/97	Uni-ZAP XR	217	999	608	999	273	273	455	1	22	23	54

Table 1 summarizes the information corresponding to each "Gene No." described above. The nucleotide sequence identified as "NT SEQ ID NO:X" was assembled from partially homologous ("overlapping") sequences obtained from the "cDNA clone ID" identified in Table 1 and, in some cases, from additional related DNA clones. The overlapping sequences were assembled into a single contiguous sequence of high redundancy (usually three to five overlapping sequences at each nucleotide position), resulting in a final sequence identified as SEQ ID NO:X.

The cDNA Clone ID was deposited on the date and given the corresponding deposit number listed in "ATCC Deposit No:Z and Date." Some of the deposits contain multiple different clones corresponding to the same gene. "Vector" refers to the type of vector contained in the cDNA Clone ID.

"Total NT Seq." refers to the total number of nucleotides in the contig identified by "Gene No." The deposited clone may contain all or most of these sequences, reflected by the nucleotide position indicated as "5' NT of Clone Seq." and the "3' NT of Clone Seq." of SEQ ID NO:X. The nucleotide position of SEQ ID NO:X of the putative start codon (methionine) is identified as "5' NT of Start Codon." Similarly , the nucleotide position of SEQ ID NO:X of the predicted signal sequence is identified as "5' NT of First AA of Signal Pep."

The translated amino acid sequence, beginning with the methionine, is identified as "AA SEQ ID NO:Y," although other reading frames can also be easily translated using known molecular biology techniques. The polypeptides produced by these alternative open reading frames are specifically contemplated by the present invention.

The first and last amino acid position of SEQ ID NO:Y of the predicted signal peptide is identified as "First AA of Sig Pep" and "Last AA of Sig Pep." The predicted first amino acid position of SEQ ID NO:Y of the secreted portion is identified as "Predicted First AA of Secreted Portion." Finally, the amino acid position of SEQ ID NO:Y of the last amino acid in the open reading frame is identified as "Last AA of ORF."

SEQ ID NO:X (where X may be any of the polynucleotide sequences disclosed in the sequence listing) and the translated SEQ ID NO:Y (where Y may be any of the polypeptide sequences disclosed in the sequence listing) are sufficiently

accurate and otherwise suitable for a variety of uses well known in the art and described further below. For instance, SEQ ID NO:X is useful for designing nucleic acid hybridization probes that will detect nucleic acid sequences contained in SEQ ID NO:X or the cDNA contained in the deposited clone. These probes will also hybridize to nucleic acid molecules in biological samples, thereby enabling a variety of forensic and diagnostic methods of the invention. Similarly, polypeptides identified from SEQ ID NO:Y may be used, for example, to generate antibodies which bind specifically to proteins containing the polypeptides and the secreted proteins encoded by the cDNA clones identified in Table 1.

Nevertheless, DNA sequences generated by sequencing reactions can contain sequencing errors. The errors exist as misidentified nucleotides, or as insertions or deletions of nucleotides in the generated DNA sequence. The erroneously inserted or deleted nucleotides cause frame shifts in the reading frames of the predicted amino acid sequence. In these cases, the predicted amino acid sequence diverges from the actual amino acid sequence, even though the generated DNA sequence may be greater than 99.9% identical to the actual DNA sequence (for example, one base insertion or deletion in an open reading frame of over 1000 bases).

Accordingly, for those applications requiring precision in the nucleotide sequence or the amino acid sequence, the present invention provides not only the generated nucleotide sequence identified as SEQ ID NO:X and the predicted translated amino acid sequence identified as SEQ ID NO:Y, but also a sample of plasmid DNA containing a human cDNA of the invention deposited with the ATCC, as set forth in Table 1. The nucleotide sequence of each deposited clone can readily be determined by sequencing the deposited clone in accordance with known methods. The predicted amino acid sequence can then be verified from such deposits. Moreover, the amino acid sequence of the protein encoded by a particular clone can also be directly determined by peptide sequencing or by expressing the protein in a suitable host cell containing the deposited human cDNA, collecting the protein, and determining its sequence.

The present invention also relates to the genes corresponding to SEQ ID NO:X, SEQ ID NO:Y, or the deposited clone. The corresponding gene can be isolated in accordance with known methods using the sequence information disclosed

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herein. Such methods include preparing probes or primers from the disclosed sequence and identifying or amplifying the corresponding gene from appropriate sources of genomic material.

Also provided in the present invention are allelic variants, orthologs, and/or species homologs. Procedures known in the art can be used to obtain full-length genes, allelic variants, splice variants, full-length coding portions, orthologs, and/or species homologs of genes corresponding to SEQ ID NO:X, SEQ ID NO:Y, or a deposited clone, using information from the sequences disclosed herein or the clones deposited with the ATCC. For example, allelic variants and/or species homologs may be isolated and identified by making suitable probes or primers from the sequences provided herein and screening a suitable nucleic acid source for allelic variants and/or the desired homologue.

The polypeptides of the invention can be prepared in any suitable manner. Such polypeptides include isolated naturally occurring polypeptides, recombinantly produced polypeptides, synthetically produced polypeptides, or polypeptides produced by a combination of these methods. Means for preparing such polypeptides are well understood in the art.

The polypeptides may be in the form of the secreted protein, including the mature form, or may be a part of a larger protein, such as a fusion protein (see below). It is often advantageous to include an additional amino acid sequence which contains secretory or leader sequences, pro-sequences, sequences which aid in purification , such as multiple histidine residues, or an additional sequence for stability during recombinant production.

The polypeptides of the present invention are preferably provided in an isolated form, and preferably are substantially purified. A recombinantly produced version of a polypeptide, including the secreted polypeptide, can be substantially purified using techniques described herein or otherwise known in the art, such as, for example, by the one-step method described in Smith and Johnson, Gene 67:31-40 (1988). Polypeptides of the invention also can be purified from natural, synthetic or recombinant sources using techniques described herein or otherwise known in the art, such as, for example, antibodies of the invention raised against the secreted protein.

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The present invention provides a polynucleotide comprising, or alternatively consisting of, the nucleic acid sequence of SEQ ID NO:X, and/or a cDNA contained in ATCC deposit Z. The present invention also provides a polypeptide comprising, or alternatively, consisting of, the polypeptide sequence of SEQ ID NO:Y and/or a polypeptide encoded by the cDNA contained in ATCC deposit Z. Polynucleotides encoding a polypeptide comprising, or alternatively consisting of the polypeptide sequence of SEQ ID NO:Y and/or a polypeptide sequence encoded by the cDNA contained in ATCC deposit Z are also encompassed by the invention.

Signal Sequences

The present invention also encompasses mature forms of the polypeptide having the polypeptide sequence of SEQ ID NO:Y and/or the polypeptide sequence encoded by the cDNA in a deposited clone. Polynucleotides encoding the mature forms (such as, for example, the polynucleotide sequence in SEQ ID NO:X and/or the polynucleotide sequence contained in the cDNA of a deposited clone) are also encompassed by the invention. According to the signal hypothesis, proteins secreted by mammalian cells have a signal or secretary leader sequence which is cleaved from the mature protein once export of the growing protein chain across the rough endoplasmic reticulum has been initiated. Most mammalian cells and even insect cells cleave secreted proteins with the same specificity. However, in some cases, cleavage of a secreted protein is not entirely uniform, which results in two or more mature species of the protein. Further, it has long been known that cleavage specificity of a secreted protein is ultimately determined by the primary structure of the complete protein, that is, it is inherent in the amino acid sequence of the polypeptide.

Methods for predicting whether a protein has a signal sequence, as well as the cleavage point for that sequence, are available. For instance, the method of McGeoch, Virus Res. 3:271-286 (1985), uses the information from a short N-terminal charged region and a subsequent uncharged region of the complete (uncleaved) protein. The method of von Heinje, Nucleic Acids Res. 14:4683-4690 (1986) uses the information from the residues surrounding the cleavage site, typically residues -13 to +2, where +1 indicates the amino terminus of the secreted protein. The accuracy of

predicting the cleavage points of known mammalian secretory proteins for each of these methods is in the range of 75-80%. (von Heinje, supra.) However, the two methods do not always produce the same predicted cleavage point(s) for a given protein.

In the present case, the deduced amino acid sequence of the secreted polypeptide was analyzed by a computer program called SignalP (Henrik Nielsen et al., Protein Engineering 10:1-6 (1997)), which predicts the cellular location of a protein based on the amino acid sequence. As part of this computational prediction of localization, the methods of McGeoch and von Heinje are incorporated. The analysis of the amino acid sequences of the secreted proteins described herein by this program provided the results shown in Table 1.

As one of ordinary skill would appreciate, however, cleavage sites sometimes vary from organism to organism and cannot be predicted with absolute certainty. Accordingly, the present invention provides secreted polypeptides having a sequence shown in SEQ ID NO:Y which have an N-terminus beginning within 5 residues (i.e., + or - 5 residues) of the predicted cleavage point. Similarly, it is also recognized that in some cases, cleavage of the signal sequence from a secreted protein is not entirely uniform, resulting in more than one secreted species. These polypeptides, and the polynucleotides encoding such polypeptides, are contemplated by the present invention.

Moreover, the signal sequence identified by the above analysis may not necessarily predict the naturally occurring signal sequence. For example, the naturally occurring signal sequence may be further upstream from the predicted signal sequence. However, it is likely that the predicted signal sequence will be capable of directing the secreted protein to the ER. Nonetheless, the present invention provides the mature protein produced by expression of the polynucleotide sequence of SEQ ID NO:X and/or the polynucleotide sequence contained in the cDNA of a deposited clone, in a mammalian cell (e.g., COS cells, as desribed below). These polypeptides, and the polynucleotides encoding such polypeptides, are contemplated by the present invention.

Polynucleotide and Polypeptide Variants

The present invention is directed to variants of the polynucleotide sequence disclosed in SEQ ID NO:X, the complementary strand thereto, and/or the cDNA sequence contained in a deposited clone.

The present invention also encompasses variants of the polypeptide sequence disclosed in SEQ ID NO:Y and/or encoded by a deposited clone.

"Variant" refers to a polynucleotide or polypeptide differing from the polynucleotide or polypeptide of the present invention, but retaining essential properties thereof. Generally, variants are overall closely similar, and, in many regions, identical to the polynucleotide or polypeptide of the present invention.

The present invention is also directed to nucleic acid molecules which comprise, or alternatively consist of, a nucleotide sequence which is at least 80%, 85%, 90%, 95%, 96%, 97%, 98% or 99% identical to, for example, the nucleotide coding sequence in SEQ ID NO:X or the complementary strand thereto, the nucleotide coding sequence contained in a deposited cDNA clone or the complementary strand thereto, a nucleotide sequence encoding the polypeptide of SEQ ID NO:Y, a nucleotide sequence encoding the polypeptide encoded by the cDNA contained in a deposited clone, and/or polynucleotide fragments of any of these nucleic acid molecules (e.g., those fragments described herein). Polynucleotides which hybridize to these nucleic acid molecules under stringent hybridization conditions or lower stringency conditions are also encompassed by the invention, as are polypeptides encoded by these polynucleotides.

The present invention is also directed to polypeptides which comprise, or alternatively consist of, an amino acid sequence which is at least 80%, 85%, 90%, 95%, 96%, 97%, 98%, 99% identical to, for example, the polypeptide sequence shown in SEQ ID NO:Y, the polypeptide sequence encoded by the cDNA contained in a deposited clone, and/or polypeptide fragments of any of these polypeptides (e.g., those fragments described herein).

By a nucleic acid having a nucleotide sequence at least, for example, 95% "identical" to a reference nucleotide sequence of the present invention, it is intended that the nucleotide sequence of the nucleic acid is identical to the reference sequence except that the nucleotide sequence may include up to five point mutations per each

100 nucleotides of the reference nucleotide sequence encoding the polypeptide. In other words, to obtain a nucleic acid having a nucleotide sequence at least 95% identical to a reference nucleotide sequence, up to 5% of the nucleotides in the reference sequence may be deleted or substituted with another nucleotide, or a number of nucleotides up to 5% of the total nucleotides in the reference sequence may be inserted into the reference sequence. The query sequence may be an entire sequence shown inTable 1, the ORF (open reading frame), or any fragment specified as described herein.

As a practical matter, whether any particular nucleic acid molecule or polypeptide is at least 80%, 85%, 90%, 95%, 96%, 97%, 98% or 99% identical to a nucleotide sequence of the presence invention can be determined conventionally using known computer programs. A preferred method for determining the best overall match between a query sequence (a sequence of the present invention) and a subject sequence, also referred to as a global sequence alignment, can be determined using the FASTDB computer program based on the algorithm of Brutlag et al. (Comp. App. Biosci. 6:237-245(1990)). In a sequence alignment the query and subject sequences are both DNA sequences. An RNA sequence can be compared by converting U's to T's. The result of said global sequence alignment is in percent identity. Preferred parameters used in a FASTDB alignment of DNA sequences to calculate percent identiy are: Matrix=Unitary, k-tuple=4, Mismatch Penalty=1, Joining Penalty=30, Randomization Group Length=0, Cutoff Score=1, Gap Penalty=5, Gap Size Penalty 0.05, Window Size=500 or the lenght of the subject nucleotide sequence, whichever is shorter.

If the subject sequence is shorter than the query sequence because of 5' or 3' deletions, not because of internal deletions, a manual correction must be made to the results. This is because the FASTDB program does not account for 5' and 3' truncations of the subject sequence when calculating percent identity. For subject sequences truncated at the 5' or 3' ends, relative to the query sequence, the percent identity is corrected by calculating the number of bases of the query sequence that are 5' and 3' of the subject sequence, which are not matched/aligned, as a percent of the total bases of the query sequence. Whether a nucleotide is matched/aligned is determined by results of the FASTDB sequence alignment. This percentage is then

subtracted from the percent identity, calculated by the above FASTDB program using the specified parameters, to arrive at a final percent identity score. This corrected score is what is used for the purposes of the present invention. Only bases outside the 5' and 3' bases of the subject sequence, as displayed by the FASTDB alignment, which are not matched/aligned with the query sequence, are calculated for the purposes of manually adjusting the percent identity score.

For example, a 90 base subject sequence is aligned to a 100 base query sequence to determine percent identity. The deletions occur at the 5' end of the subject sequence and therefore, the FASTDB alignment does not show a matched/alignment of the first 10 bases at 5' end. The 10 unpaired bases represent 10% of the sequence (number of bases at the 5' and 3' ends not matched/total number of bases in the query sequence) so 10% is subtracted from the percent identity score calculated by the FASTDB program. If the remaining 90 bases were perfectly matched the final percent identity would be 90%. In another example, a 90 base subject sequence is compared with a 100 base query sequence. This time the deletions are internal deletions so that there are no bases on the 5' or 3' of the subject sequence which are not matched/aligned with the query. In this case the percent identity calculated by FASTDB is not manually corrected. Once again, only bases 5' and 3' of the subject sequence which are not matched/aligned with the query sequence are manually corrected for. No other manual corrections are to made for the purposes of the present invention.

By a polypeptide having an amino acid sequence at least, for example, 95% "identical" to a query amino acid sequence of the present invention, it is intended that the amino acid sequence of the subject polypeptide is identical to the query sequence except that the subject polypeptide sequence may include up to five amino acid alterations per each 100 amino acids of the query amino acid sequence. In other words, to obtain a polypeptide having an amino acid sequence at least 95% identical to a query amino acid sequence, up to 5% of the amino acid residues in the subject sequence may be inserted, deleted, (indels) or substituted with another amino acid. These alterations of the reference sequence may occur at the amino or carboxy terminal positions of the reference amino acid sequence or anywhere between those terminal positions, interspersed either individually among residues in the reference

sequence or in one or more contiguous groups within the reference sequence.

As a practical matter, whether any particular polypeptide is at least 80%, 85%, 90%, 95%, 96%, 97%, 98% or 99% identical to, for instance, an amino acid sequences shown in Table 1 (SEQ ID NO:Y) or to the amino acid sequence encoded by cDNA contained in a deposited clone can be determined conventionally using known computer programs. A preferred method for determing the best overall match between a query sequence (a sequence of the present invention) and a subject sequence, also referred to as a global sequence alignment, can be determined using the FASTDB computer program based on the algorithm of Brutlag et al. (Comp. App. Biosci. 6:237-245(1990)). In a sequence alignment the query and subject sequences are either both nucleotide sequences or both amino acid sequences. The result of said global sequence alignment is in percent identity. Preferred parameters used in a FASTDB amino acid alignment are: Matrix=PAM 0, k-tuple=2, Mismatch Penalty=1, Joining Penalty=20, Randomization Group Length=0, Cutoff Score=1, Window Size=sequence length, Gap Penalty=5, Gap Size Penalty=0.05, Window Size=500 or the length of the subject amino acid sequence, whichever is shorter.

If the subject sequence is shorter than the query sequence due to N- or C-terminal deletions, not because of internal deletions, a manual correction must be made to the results. This is because the FASTDB program does not account for N- and C-terminal truncations of the subject sequence when calculating global percent identity. For subject sequences truncated at the N- and C-termini, relative to the query sequence, the percent identity is corrected by calculating the number of residues of the query sequence that are N- and C-terminal of the subject sequence, which are not matched/aligned with a corresponding subject residue, as a percent of the total bases of the query sequence. Whether a residue is matched/aligned is determined by results of the FASTDB sequence alignment. This percentage is then subtracted from the percent identity, calculated by the above FASTDB program using the specified parameters, to arrive at a final percent identity score. This final percent identity score is what is used for the purposes of the present invention. Only residues to the N- and C-termini of the subject sequence, which are not matched/aligned with the query sequence, are considered for the purposes of manually adjusting the percent identity score. That is, only query residue positions outside the farthest N- and C-terminal

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residues of the subject sequence.

For example, a 90 amino acid residue subject sequence is aligned with a 100 residue query sequence to determine percent identity. The deletion occurs at the N-terminus of the subject sequence and therefore, the FASTDB alignment does not show a matching/alignment of the first 10 residues at the N-terminus. The 10 unpaired residues represent 10% of the sequence (number of residues at the N- and C-termini not matched/total number of residues in the query sequence) so 10% is subtracted from the percent identity score calculated by the FASTDB program. If the remaining 90 residues were perfectly matched the final percent identity would be 90%. In another example, a 90 residue subject sequence is compared with a 100 residue query sequence. This time the deletions are internal deletions so there are no residues at the N- or C-termini of the subject sequence which are not matched/aligned with the query. In this case the percent identity calculated by FASTDB is not manually corrected. Once again, only residue positions outside the N- and C-terminal ends of the subject sequence, as displayed in the FASTDB alignment, which are not matched/aligned with the query sequnce are manually corrected for. No other manual corrections are to made for the purposes of the present invention.

The variants may contain alterations in the coding regions, non-coding regions, or both. Especially preferred are polynucleotide variants containing alterations which produce silent substitutions, additions, or deletions, but do not alter the properties or activities of the encoded polypeptide. Nucleotide variants produced by silent substitutions due to the degeneracy of the genetic code are preferred. Moreover, variants in which 5-10, 1-5, or 1-2 amino acids are substituted, deleted, or added in any combination are also preferred. Polynucleotide variants can be produced for a variety of reasons, e.g., to optimize codon expression for a particular host (change codons in the human mRNA to those preferred by a bacterial host such as E. coli).

Naturally occurring variants are called "allelic variants," and refer to one of several alternate forms of a gene occupying a given locus on a chromosome of an organism. (Genes II, Lewin, B., ed., John Wiley & Sons, New York (1985).) These allelic variants can vary at either the polynucleotide and/or polypeptide level and are

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included in the present invention. Alternatively, non-naturally occurring variants may be produced by mutagenesis techniques or by direct synthesis.

Using known methods of protein engineering and recombinant DNA technology, variants may be generated to improve or alter the characteristics of the polypeptides of the present invention. For instance, one or more amino acids can be deleted from the N-terminus or C-terminus of the secreted protein without substantial loss of biological function. The authors of Ron et al., J. Biol. Chem. 268: 2984-2988 (1993), reported variant KGF proteins having heparin binding activity even after deleting 3, 8, or 27 amino-terminal amino acid residues. Similarly, Interferon gamma exhibited up to ten times higher activity after deleting 8-10 amino acid residues from the carboxy terminus of this protein. (Dobeli et al., J. Biotechnology 7:199-216 (1988).)

Moreover, ample evidence demonstrates that variants often retain a biological activity similar to that of the naturally occurring protein. For example, Gayle and coworkers (J. Biol. Chem 268:22105-22111 (1993)) conducted extensive mutational analysis of human cytokine IL-1a. They used random mutagenesis to generate over 3,500 individual IL-1a mutants that averaged 2.5 amino acid changes per variant over the entire length of the molecule. Multiple mutations were examined at every possible amino acid position. The investigators found that "[m]ost of the molecule could be altered with little effect on either [binding or biological activity]." (See, Abstract.) In fact, only 23 unique amino acid sequences, out of more than 3,500 nucleotide sequences examined, produced a protein that significantly differed in activity from wild-type.

Furthermore, even if deleting one or more amino acids from the N-terminus or C-terminus of a polypeptide results in modification or loss of one or more biological functions, other biological activities may still be retained. For example, the ability of a deletion variant to induce and/or to bind antibodies which recognize the secreted form will likely be retained when less than the majority of the residues of the secreted form are removed from the N-terminus or C-terminus. Whether a particular polypeptide lacking N- or C-terminal residues of a protein retains such immunogenic activities can readily be determined by routine methods described herein and otherwise known in the art.

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Thus, the invention further includes polypeptide variants which show substantial biological activity. Such variants include deletions, insertions, inversions, repeats, and substitutions selected according to general rules known in the art so as have little effect on activity. For example, guidance concerning how to make phenotypically silent amino acid substitutions is provided in Bowie et al., Science 247:1306-1310 (1990), wherein the authors indicate that there are two main strategies for studying the tolerance of an amino acid sequence to change.

The first strategy exploits the tolerance of amino acid substitutions by natural selection during the process of evolution. By comparing amino acid sequences in different species, conserved amino acids can be identified. These conserved amino acids are likely important for protein function. In contrast, the amino acid positions where substitutions have been tolerated by natural selection indicates that these positions are not critical for protein function. Thus, positions tolerating amino acid substitution could be modified while still maintaining biological activity of the protein.

The second strategy uses genetic engineering to introduce amino acid changes at specific positions of a cloned gene to identify regions critical for protein function. For example, site directed mutagenesis or alanine-scanning mutagenesis (introduction of single alanine mutations at every residue in the molecule) can be used. (Cunningham and Wells, Science 244:1081-1085 (1989).) The resulting mutant molecules can then be tested for biological activity.

As the authors state, these two strategies have revealed that proteins are surprisingly tolerant of amino acid substitutions. The authors further indicate which amino acid changes are likely to be permissive at certain amino acid positions in the protein. For example, most buried (within the tertiary structure of the protein) amino acid residues require nonpolar side chains, whereas few features of surface side chains are generally conserved. Moreover, tolerated conservative amino acid substitutions involve replacement of the aliphatic or hydrophobic amino acids Ala, Val, Leu and Ile; replacement of the hydroxyl residues Ser and Thr; replacement of the acidic residues Asp and Glu; replacement of the amide residues Asn and Gln, replacement of the basic residues Lys, Arg, and His; replacement of the aromatic residues Phe, Tyr, and Trp, and replacement of the small-sized amino acids Ala, Ser, Thr, Met, and Gly.

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Besides conservative amino acid substitution, variants of the present invention include (i) substitutions with one or more of the non-conserved amino acid residues, where the substituted amino acid residues may or may not be one encoded by the genetic code, or (ii) substitution with one or more of amino acid residues having a substituent group, or (iii) fusion of the mature polypeptide with another compound, such as a compound to increase the stability and/or solubility of the polypeptide (for example, polyethylene glycol), or (iv) fusion of the polypeptide with additional amino acids, such as, for example, an IgG Fc fusion region peptide, or leader or secretory sequence, or a sequence facilitating purification or (v) fusion of the polypeptide with another compound, such as albumin (including, but not limited to, recombinant albumin (see, e.g., U.S. Patent No. 5,876,969, issued March 2, 1999, EP Patent 0 413 622, and U.S. Patent No. 5,766,883, issued June 16, 1998, herein incorporated by reference in their entirety)). Such variant polypeptides are deemed to be within the scope of those skilled in the art from the teachings herein.

For example, polypeptide variants containing amino acid substitutions of charged amino acids with other charged or neutral amino acids may produce proteins with improved characteristics, such as less aggregation. Aggregation of pharmaceutical formulations both reduces activity and increases clearance due to the aggregate's immunogenic activity. (Pinckard et al., Clin. Exp. Immunol. 2:331-340 (1967); Robbins et al., Diabetes 36: 838-845 (1987); Cleland et al., Crit. Rev. Therapeutic Drug Carrier Systems 10:307-377 (1993).)

A further embodiment of the invention relates to a polypeptide which comprises the amino acid sequence of the present invention having an amino acid sequence which contains at least one amino acid substitution, but not more than 50 amino acid substitutions, even more preferably, not more than 40 amino acid substitutions, still more preferably, not more than 30 amino acid substitutions, and still even more preferably, not more than 20 amino acid substitutions. Of course, in order of ever-increasing preference, it is highly preferable for a peptide or polypeptide to have an amino acid sequence which comprises the amino acid sequence of the present invention, which contains at least one, but not more than 10, 9, 8, 7, 6, 5, 4, 3, 2 or 1 amino acid substitutions. In specific embodiments, the number of additions, substitutions, and/or deletions in the amino acid sequence of the present invention or

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fragments thereof (e.g., the mature form and/or other fragments described herein), is 1-5, 5-10, 5-25, 5-50, 10-50 or 50-150, conservative amino acid substitutions are preferable.

Polynucleotide and Polypeptide Fragments

The present invention is also directed to polynucleotide fragments of the polynucleotides of the invention.

In the present invention, a "polynucleotide fragment" refers to a short polynucleotide having a nucleic acid sequence which: is a portion of that contained in a deposited clone, or encoding the polypeptide encoded by the cDNA in a deposited clone; is a portion of that shown in SEQ ID NO:X or the complementary strand thereto, or is a portion of a polynucleotide sequence encoding the polypeptide of SEQ ID NO:Y. The nucleotide fragments of the invention are preferably at least about 15 nt, and more preferably at least about 20 nt, still more preferably at least about 30 nt, and even more preferably, at least about 40 nt, at least about 50 nt, at least about 75 nt, or at least about 150 nt in length. A fragment "at least 20 nt in length," for example, is intended to include 20 or more contiguous bases from the cDNA sequence contained in a deposited clone or the nucleotide sequence shown in SEQ ID NO:X. In this context "about" includes the particularly recited value, a value larger or smaller by several (5, 4, 3, 2, or 1) nucleotides, at either terminus or at both termini. These nucleotide fragments have uses that include, but are not limited to, as diagnostic probes and primers as discussed herein. Of course, larger fragments (e.g., 50, 150, 500, 600, 2000 nucleotides) are preferred.

Moreover, representative examples of polynucleotide fragments of the invention, include, for example, fragments comprising, or alternatively consisting of, a sequence from about nucleotide number 1-50, 51-100, 101-150, 151-200, 201-250, 251-300, 301-350, 351-400, 401-450, 451-500, 501-550, 551-600, 651-700, 701-750, 751-800, 800-850, 851-900, 901-950, 951-1000, 1001-1050, 1051-1100, 1101-1150, 1151-1200, 1201-1250, 1251-1300, 1301-1350, 1351-1400, 1401-1450, 1451-1500, 1501-1550, 1551-1600, 1601-1650, 1651-1700, 1701-1750, 1751-1800, 1801-1850, 1851-1900, 1901-1950, 1951-2000, or 2001 to the end of SEQ ID NO:X, or the complementary strand thereto, or the cDNA contained in a deposited clone. In this

context "about" includes the particularly recited ranges, and ranges larger or smaller by several (5, 4, 3, 2, or 1) nucleotides, at either terminus or at both termini. Preferably, these fragments encode a polypeptide which has biological activity. More preferably, these polynucleotides can be used as probes or primers as discussed herein. Polynucleotides which hybridize to these nucleic acid molecules under stringent hybridization conditions or lower stringency conditions are also encompassed by the invention, as are polypeptides encoded by these polynucleotides.

In the present invention, a "polypeptide fragment" refers to an amino acid sequence which is a portion of that contained in SEQ ID NO:Y or encoded by the cDNA contained in a deposited clone. Protein (polypeptide) fragments may be "free-standing," or comprised within a larger polypeptide of which the fragment forms a part or region, most preferably as a single continuous region. Representative examples of polypeptide fragments of the invention, include, for example, fragments comprising, or alternatively consisting of, from about amino acid number 1-20, 21-40, 41-60, 61-80, 81-100, 102-120, 121-140, 141-160, or 161 to the end of the coding region. Moreover, polypeptide fragments can be about 20, 30, 40, 50, 60, 70, 80, 90, 100, 110, 120, 130, 140, or 150 amino acids in length. In this context "about" includes the particularly recited ranges or values, and ranges or values larger or smaller by several (5, 4, 3, 2, or 1) amino acids, at either extreme or at both extremes. Polynucleotides encoding these polypeptides are also encompassed by the invention.

Preferred polypeptide fragments include the secreted protein as well as the mature form. Further preferred polypeptide fragments include the secreted protein or the mature form having a continuous series of deleted residues from the amino or the carboxy terminus, or both. For example, any number of amino acids, ranging from 1-60, can be deleted from the amino terminus of either the secreted polypeptide or the mature form. Similarly, any number of amino acids, ranging from 1-30, can be deleted from the carboxy terminus of the secreted protein or mature form. Furthermore, any combination of the above amino and carboxy terminus deletions are preferred. Similarly, polynucleotides encoding these polypeptide fragments are also preferred.

Also preferred are polypeptide and polynucleotide fragments characterized by structural or functional domains, such as fragments that comprise alpha-helix and

alpha-helix forming regions, beta-sheet and beta-sheet-forming regions, turn and turn-forming regions, coil and coil-forming regions, hydrophilic regions, hydrophobic regions, alpha amphipathic regions, beta amphipathic regions, flexible regions, surface-forming regions, substrate binding region, and high antigenic index regions. Polypeptide fragments of SEQ ID NO:Y falling within conserved domains are specifically contemplated by the present invention. Moreover, polynucleotides encoding these domains are also contemplated.

Other preferred polypeptide fragments are biologically active fragments. Biologically active fragments are those exhibiting activity similar, but not necessarily identical, to an activity of the polypeptide of the present invention. The biological activity of the fragments may include an improved desired activity, or a decreased undesirable activity. Polynucleotides encoding these polypeptide fragments are also encompassed by the invention.

Preferably, the polynucleotide fragments of the invention encode a polypeptide which demonstrates a functional activity. By a polypeptide demonstrating a "functional activity" is meant, a polypeptide capable of displaying one or more known functional activities associated with a full-length (complete) polypeptide of invention protein. Such functional activities include, but are not limited to, biological activity, antigenicity [ability to bind (or compete with a polypeptide of the invention for binding) to an antibody to the polypeptide of the invention], immunogenicity (ability to generate antibody which binds to a polypeptide of the invention), ability to form multimers with polypeptides of the invention, and ability to bind to a receptor or ligand for a polypeptide of the invention.

The functional activity of polypeptides of the invention, and fragments, variants derivatives, and analogs thereof, can be assayed by various methods.

For example, in one embodiment where one is assaying for the ability to bind or compete with full-length polypeptide of the invention for binding to an antibody of the polypeptide of the invention, various immunoassays known in the art can be used, including but not limited to, competitive and non-competitive assay systems using techniques such as radioimmunoassays, ELISA (enzyme linked immunosorbent assay), "sandwich" immunoassays, immunoradiometric assays, gel diffusion precipitation reactions, immunodiffusion assays, in situ immunoassays (using

colloidal gold, enzyme or radioisotope labels, for example), western blots, precipitation reactions, agglutination assays (e.g., gel agglutination assays, hemagglutination assays), complement fixation assays, immunofluorescence assays, protein A assays, and immunoelectrophoresis assays, etc. In one embodiment, antibody binding is detected by detecting a label on the primary antibody. In another embodiment, the primary antibody is detected by detecting binding of a secondary antibody or reagent to the primary antibody. In a further embodiment, the secondary antibody is labeled. Many means are known in the art for detecting binding in an immunoassay and are within the scope of the present invention.

In another embodiment, where a ligand for a polypeptide of the invention identified, or the ability of a polypeptide fragment, variant or derivative of the invention to multimerize is being evaluated, binding can be assayed, e.g., by means well-known in the art, such as, for example, reducing and non-reducing gel chromatography, protein affinity chromatography, and affinity blotting. See generally, Phizicky, E., et al., 1995, Microbiol. Rev. 59:94-123. In another embodiment, physiological correlates of binding of a polypeptide of the invention to its substrates (signal transduction) can be assayed.

In addition, assays described herein (see Examples) and otherwise known in the art may routinely be applied to measure the ability of polypeptides of the invention and fragments, variants derivatives and analogs thereof to elicit related biological activity related to that of the polypeptide of the invention (either in vitro or in vivo). Other methods will be known to the skilled artisan and are within the scope of the invention.

Epitopes and Antibodies

The present invention encompasses polypeptides comprising, or alternatively consisting of, an epitope of the polypeptide having an amino acid sequence of SEQ ID NO:Y, or an epitope of the polypeptide sequence encoded by a polynucleotide sequence contained in ATCC deposit No. Z or encoded by a polynucleotide that hybridizes to the complement of the sequence of SEQ ID NO:X or contained in ATCC deposit No. Z under stringent hybridization conditions or lower stringency hybridization conditions as defined supra. The present invention further encompasses

polynucleotide sequences encoding an epitope of a polypeptide sequence of the invention (such as, for example, the sequence disclosed in SEQ ID NO:X), polynucleotide sequences of the complementary strand of a polynucleotide sequence encoding an epitope of the invention, and polynucleotide sequences which hybridize to the complementary strand under stringent hybridization conditions or lower stringency hybridization conditions defined supra.

The term "epitopes," as used herein, refers to portions of a polypeptide having antigenic or immunogenic activity in an animal, preferably a mammal, and most preferably in a human. In a preferred embodiment, the present invention encompasses a polypeptide comprising an epitope, as well as the polynucleotide encoding this polypeptide. An "immunogenic epitope," as used herein, is defined as a portion of a protein that elicits an antibody response in an animal, as determined by any method known in the art, for example, by the methods for generating antibodies described infra. (See, for example, Geysen et al., Proc. Natl. Acad. Sci. USA 81:3998- 4002 (1983)). The term "antigenic epitope," as used herein, is defined as a portion of a protein to which an antibody can immunospecifically bind its antigen as determined by any method well known in the art, for example, by the immunoassays described herein. Immunospecific binding excludes non-specific binding but does not necessarily exclude cross- reactivity with other antigens. Antigenic epitopes need not necessarily be immunogenic.

Fragments which function as epitopes may be produced by any conventional means. (See, e.g., Houghten, Proc. Natl. Acad. Sci. USA 82:5131-5135 (1985), further described in U.S. Patent No. 4,631,211).

In the present invention, antigenic epitopes preferably contain a sequence of at least 4, at least 5, at least 6, at least 7, more preferably at least 8, at least 9, at least 10, at least 11, at least 12, at least 13, at least 14, at least 15, at least 20, at least 25, at least 30, at least 40, at least 50, and, most preferably, between about 15 to about 30 amino acids. Preferred polypeptides comprising immunogenic or antigenic epitopes are at least 10, 15, 20, 25, 30, 35, 40, 45, 50, 55, 60, 65, 70, 75, 80, 85, 90, 95, or 100 amino acid residues in length. Additional non-exclusive preferred antigenic epitopes include the antigenic epitopes disclosed herein, as well as portions thereof. Antigenic epitopes are useful, for example, to raise antibodies, including monoclonal antibodies,

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that specifically bind the epitope. Preferred antigenic epitopes include the antigenic epitopes disclosed herein, as well as any combination of two, three, four, five or more of these antigenic epitopes. Antigenic epitopes can be used as the target molecules in immunoassays. (See, for instance, Wilson et al., Cell 37:767-778 (1984); Sutcliffe et al., Science 219:660-666 (1983)).

Similarly, immunogenic epitopes can be used, for example, to induce antibodies according to methods well known in the art. (See, for instance, Sutcliffe et al., supra; Wilson et al., supra; Chow et al., Proc. Natl. Acad. Sci. USA 82:910-914; and Bittle et al., J. Gen. Virol. 66:2347-2354 (1985). Preferred immunogenic epitopes include the immunogenic epitopes disclosed herein, as well as any combination of two, three, four, five or more of these immunogenic epitopes. The polypeptides comprising one or more immunogenic epitopes may be presented for eliciting an antibody response together with a carrier protein, such as an albumin, to an animal system (such as rabbit or mouse), or, if the polypeptide is of sufficient length (at least about 25 amino acids), the polypeptide may be presented without a carrier. However, immunogenic epitopes comprising as few as 8 to 10 amino acids have been shown to be sufficient to raise antibodies capable of binding to, at the very least, linear epitopes in a denatured polypeptide (e.g., in Western blotting).

Epitope-bearing polypeptides of the present invention may be used to induce antibodies according to methods well known in the art including, but not limited to, in vivo immunization, in vitro immunization, and phage display methods. See, e.g., Sutcliffe et al., supra; Wilson et al., supra, and Bittle et al., J. Gen. Virol., 66:2347-2354 (1985). If in vivo immunization is used, animals may be immunized with free peptide; however, anti-peptide antibody titer may be boosted by coupling the peptide to a macromolecular carrier, such as keyhole limpet hemacyanin (KLH) or tetanus toxoid. For instance, peptides containing cysteine residues may be coupled to a carrier using a linker such as maleimidobenzoyl- N-hydroxysuccinimide ester (MBS), while other peptides may be coupled to carriers using a more general linking agent such as glutaraldehyde. Animals such as rabbits, rats and mice are immunized with either free or carrier- coupled peptides, for instance, by intraperitoneal and/or intradermal injection of emulsions containing about 100 μg of peptide or carrier protein and Freund's adjuvant or any other adjuvant known for stimulating an

immune response. Several booster injections may be needed, for instance, at intervals of about two weeks, to provide a useful titer of anti-peptide antibody which can be detected, for example, by ELISA assay using free peptide adsorbed to a solid surface. The titer of anti-peptide antibodies in serum from an immunized animal may be increased by selection of anti-peptide antibodies, for instance, by adsorption to the peptide on a solid support and elution of the selected antibodies according to methods well known in the art.

As one of skill in the art will appreciate, and as discussed above, the polypeptides of the present invention (e.g., those comprising an immunogenic or antigenic epitope) can be fused to heterologous polypeptide sequences. For example, polypeptides of the present invention (including fragments or variants thereof), may be fused with the constant domain of immunoglobulins (IgA, IgE, IgG, IgM), or portions thereof (CH1, CH2, CH3, or any combination thereof and portions thereof, resulting in chimeric polypeptides. By way of another non-limiting example, polypeptides and/or antibodies of the present invention (including fragments or variants thereof) may be fused with albumin (including but not limited to recombinant human serum albumin or fragments or variants thereof (see, e.g., U.S. Patent No. 5,876,969, issued March 2, 1999, EP Patent 0 413 622, and U.S. Patent No. 5,766,883, issued June 16, 1998, herein incorporated by reference in their entirety)). In a preferred embodiment, polypeptides and/or antibodies of the present invention (including fragments or variants thereof) are fused with the mature form of human serum albumin (i.e., amino acids 1 – 585 of human serum albumin as shown in Figures 1 and 2 of EP Patent 0 322 094) which is herein incorporated by reference in its entirety. In another preferred embodiment, polypeptides and/or antibodies of the present invention (including fragments or variants thereof) are fused with polypeptide fragments comprising, or alternatively consisting of, amino acid residues 1-z of human serum albumin, where z is an integer from 369 to 419, as described in U.S. Patent 5,766,883 herein incorporated by reference in its entirety. Polypeptides and/or antibodies of the present invention (including fragments or variants thereof) may be fused to either the N- or C-terminal end of the heterologous protein (e.g., immunoglobulin Fc polypeptide or human serum albumin polypeptide).

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Polynucleotides encoding fusion proteins of the invention are also encompassed by the invention.

Such fusion proteins may facilitate purification and may increase half-life in vivo. This has been shown for chimeric proteins consisting of the first two domains of the human CD4-polypeptide and various domains of the constant regions of the heavy or light chains of mammalian immunoglobulins. See, e.g., EP 394,827; Traunecker et al., Nature, 331:84-86 (1988). Enhanced delivery of an antigen across the epithelial barrier to the immune system has been demonstrated for antigens (e.g., insulin) conjugated to an FcRn binding partner such as IgG or Fc fragments (see, e.g., PCT Publications WO 96/22024 and WO 99/04813). IgG Fusion proteins that have a disulfide-linked dimeric structure due to the IgG portion desulfide bonds have also been found to be more efficient in binding and neutralizing other molecules than monomeric polypeptides or fragments thereof alone. See, e.g., Fountoulakis et al., J. Biochem., 270:3958-3964 (1995). Nucleic acids encoding the above epitopes can also be recombined with a gene of interest as an epitope tag (e.g., the hemagglutinin ("HA") tag or flag tag) to aid in detection and purification of the expressed polypeptide. For example, a system described by Janknecht et al. allows for the ready purification of non-denatured fusion proteins expressed in human cell lines (Janknecht et al., 1991, Proc. Natl. Acad. Sci. USA 88:8972- 897). In this system, the gene of interest is subcloned into a vaccinia recombination plasmid such that the open reading frame of the gene is translationally fused to an amino-terminal tag consisting of six histidine residues. The tag serves as a matrix binding domain for the fusion protein. Extracts from cells infected with the recombinant vaccinia virus are loaded onto Ni2+ nitriloacetic acid-agarose column and histidine-tagged proteins can be selectively eluted with imidazole-containing buffers.

Additional fusion proteins of the invention may be generated through the techniques of gene-shuffling, motif-shuffling, exon-shuffling, and/or codon-shuffling (collectively referred to as "DNA shuffling"). DNA shuffling may be employed to modulate the activities of polypeptides of the invention, such methods can be used to generate polypeptides with altered activity, as well as agonists and antagonists of the polypeptides. See, generally, U.S. Patent Nos. 5,605,793; 5,811,238; 5,830,721; 5,834,252; and 5,837,458, and Patten et al., Curr. Opinion Biotechnol. 8:724-33

(1997); Harayama, Trends Biotechnol. 16(2):76-82 (1998); Hansson, et al., J. Mol. Biol. 287:265-76 (1999); and Lorenzo and Blasco, Biotechniques 24(2):308- 13 (1998) (each of these patents and publications are hereby incorporated by reference in its entirety). In one embodiment, alteration of polynucleotides corresponding to SEQ ID NO:X and the polypeptides encoded by these polynucleotides may be achieved by DNA shuffling. DNA shuffling involves the assembly of two or more DNA segments by homologous or site-specific recombination to generate variation in the polynucleotide sequence. In another embodiment, polynucleotides of the invention, or the encoded polypeptides, may be altered by being subjected to random mutagenesis by error-prone PCR, random nucleotide insertion or other methods prior to recombination. In another embodiment, one or more components, motifs, sections, parts, domains, fragments, etc., of a polynucleotide encoding a polypeptide of the invention may be recombined with one or more components, motifs, sections, parts, domains, fragments, etc. of one or more heterologous molecules.

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Antibodies

Further polypeptides of the invention relate to antibodies and T-cell antigen receptors (TCR) which immunospecifically bind a polypeptide, polypeptide fragment, or variant of SEQ ID NO:Y, and/or an epitope, of the present invention (as determined by immunoassays well known in the art for assaying specific antibody-antigen binding). Antibodies of the invention include, but are not limited to, polyclonal, monoclonal, multispecific, human, humanized or chimeric antibodies, single chain antibodies, Fab fragments, F(ab') fragments, fragments produced by a Fab expression library, anti-idiotypic (anti-Id) antibodies (including, e.g., anti-Id antibodies to antibodies of the invention), and epitope-binding fragments of any of the above. The term "antibody," as used herein, refers to immunoglobulin molecules and immunologically active portions of immunoglobulin molecules, i.e., molecules that contain an antigen binding site that immunospecifically binds an antigen. The immunoglobulin molecules of the invention can be of any type (e.g., IgG, IgE, IgM, IgD, IgA and IgY), class (e.g., IgG1, IgG2, IgG3, IgG4, IgA1 and IgA2) or subclass of immunoglobulin molecule. In preferred embodiments, the immunoglobulin

molecules of the invention are IgG1. In other preferred embodiments, the immunoglobulin molecules of the invention are IgG4.

Most preferably the antibodies are human antigen-binding antibody fragments of the present invention and include, but are not limited to, Fab, Fab' and F(ab')2, Fd, single-chain Fvs (scFv), single-chain antibodies, disulfide-linked Fvs (sdFv) and fragments comprising either a VL or VH domain. Antigen-binding antibody fragments, including single-chain antibodies, may comprise the variable region(s) alone or in combination with the entirety or a portion of the following: hinge region, CH1, CH2, and CH3 domains. Also included in the invention are antigen-binding fragments also comprising any combination of variable region(s) with a hinge region, CH1, CH2, and CH3 domains. The antibodies of the invention may be from any animal origin including birds and mammals. Preferably, the antibodies are human, murine (e.g., mouse and rat), donkey, ship rabbit, goat, guinea pig, camel, horse, or chicken. As used herein, "human" antibodies include antibodies having the amino acid sequence of a human immunoglobulin and include antibodies isolated from human immunoglobulin libraries or from animals transgenic for one or more human immunoglobulin and that do not express endogenous immunoglobulins, as described infra and, for example in, U.S. Patent No. 5,939,598 by Kucherlapati et al.

The antibodies of the present invention may be monospecific, bispecific, trispecific or of greater multispecificity. Multispecific antibodies may be specific for different epitopes of a polypeptide of the present invention or may be specific for both a polypeptide of the present invention as well as for a heterologous epitope, such as a heterologous polypeptide or solid support material. See, e.g., PCT publications WO 93/17715; WO 92/08802; WO 91/00360; WO 92/05793; Tutt, et al., J. Immunol. 147:60-69 (1991); U.S. Patent Nos. 4,474,893; 4,714,681; 4,925,648; 5,573,920; 5,601,819; Kostelny et al., J. Immunol. 148:1547-1553 (1992).

Antibodies of the present invention may be described or specified in terms of the epitope(s) or portion(s) of a polypeptide of the present invention which they recognize or specifically bind. The epitope(s) or polypeptide portion(s) may be specified as described herein, e.g., by N-terminal and C-terminal positions, by size in contiguous amino acid residues, or listed in the Tables and Figures. Antibodies which specifically bind any epitope or polypeptide of the present invention may also be

excluded. Therefore, the present invention includes antibodies that specifically bind polypeptides of the present invention, and allows for the exclusion of the same.

Antibodies of the present invention may also be described or specified in terms of their cross-reactivity. Antibodies that do not bind any other analog, ortholog, or homolog of a polypeptide of the present invention are included. Antibodies that bind polypeptides with at least 95%, at least 90%, at least 85%, at least 80%, at least 75%, at least 70%, at least 65%, at least 60%, at least 55%, and at least 50% identity (as calculated using methods known in the art and described herein) to a polypeptide of the present invention are also included in the present invention. In specific embodiments, antibodies of the present invention cross-react with murine, rat and/or rabbit homologs of human proteins and the corresponding epitopes thereof. Antibodies that do not bind polypeptides with less than 95%, less than 90%, less than 85%, less than 80%, less than 75%, less than 70%, less than 65%, less than 60%, less than 55%, and less than 50% identity (as calculated using methods known in the art and described herein) to a polypeptide of the present invention are also included in the present invention. In a specific embodiment, the above-described cross-reactivity is with respect to any single specific antigenic or immunogenic polypeptide, or combination(s) of 2, 3, 4, 5, or more of the specific antigenic and/or immunogenic polypeptides disclosed herein. Further included in the present invention are antibodies which bind polypeptides encoded by polynucleotides which hybridize to a polynucleotide of the present invention under stringent hybridization conditions (as described herein). Antibodies of the present invention may also be described or specified in terms of their binding affinity to a polypeptide of the invention. Preferred binding affinities include those with a dissociation constant or Kd less than 5×10^{-2} M, 10^{-2} M, 5×10^{-3} M, 10^{-3} M, 5×10^{-4} M, 10^{-4} M, 5×10^{-5} M, 10^{-5} M, 5×10^{-6} M, 10^{-6}M, 5×10^{-7} M, 10^{7} M, 5×10^{-8} M, 10^{-8} M, 5×10^{-9} M, 10^{-9} M, 5×10^{-10} M, 10^{-10} M, 5×10^{-11} M, 10^{-11} M, 5×10^{-12} M, $^{10-12}$ M, 5×10^{-13} M, 10^{-13} M, 5×10^{-14} M, 10^{-14} M, 5×10^{-15} M, or 10^{-15} M.

The invention also provides antibodies that competitively inhibit binding of an antibody to an epitope of the invention as determined by any method known in the art for determining competitive binding, for example, the immunoassays described herein. In preferred embodiments, the antibody competitively inhibits binding to the

epitope by at least 95%, at least 90%, at least 85 %, at least 80%, at least 75%, at least 70%, at least 60%, or at least 50%.

Antibodies of the present invention may act as agonists or antagonists of the polypeptides of the present invention. For example, the present invention includes antibodies which disrupt the receptor/ligand interactions with the polypeptides of the invention either partially or fully. Preferrably, antibodies of the present invention bind an antigenic epitope disclosed herein, or a portion thereof. The invention features both receptor-specific antibodies and ligand-specific antibodies. The invention also features receptor-specific antibodies which do not prevent ligand binding but prevent receptor activation. Receptor activation (i.e., signaling) may be determined by techniques described herein or otherwise known in the art. For example, receptor activation can be determined by detecting the phosphorylation (e.g., tyrosine or serine/threonine) of the receptor or its substrate by immunoprecipitation followed by western blot analysis (for example, as described supra). In specific embodiments, antibodies are provided that inhibit ligand activity or receptor activity by at least 95%, at least 90%, at least 85%, at least 80%, at least 75%, at least 70%, at least 60%, or at least 50% of the activity in absence of the antibody.

The invention also features receptor-specific antibodies which both prevent ligand binding and receptor activation as well as antibodies that recognize the receptor-ligand complex, and, preferably, do not specifically recognize the unbound receptor or the unbound ligand. Likewise, included in the invention are neutralizing antibodies which bind the ligand and prevent binding of the ligand to the receptor, as well as antibodies which bind the ligand, thereby preventing receptor activation, but do not prevent the ligand from binding the receptor. Further included in the invention are antibodies which activate the receptor. These antibodies may act as receptor agonists, i.e., potentiate or activate either all or a subset of the biological activities of the ligand-mediated receptor activation, for example, by inducing dimerization of the receptor. The antibodies may be specified as agonists, antagonists or inverse agonists for biological activities comprising the specific biological activities of the peptides of the invention disclosed herein. The above antibody agonists can be made using methods known in the art. See, e.g., PCT publication WO 96/40281; U.S. Patent No.

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5,811,097; Deng et al., Blood 92(6):1981-1988 (1998); Chen et al., Cancer Res. 58(16):3668-3678 (1998); Harrop et al., J. Immunol. 161(4):1786-1794 (1998); Zhu et al., Cancer Res. 58(15):3209-3214 (1998); Yoon et al., J. Immunol. 160(7):3170-3179 (1998); Prat et al., J. Cell. Sci. 111(Pt2):237-247 (1998); Pitard et al., J. Immunol. Methods 205(2):177-190 (1997); Liautārd et al., Cytokine 9(4):233-241 (1997); Carlson et al., J. Biol. Chem. 272(17):11295-11301 (1997); Taryman et al., Neuron 14(4):755-762 (1995); Muller et al., Structure 6(9):1153-1167 (1998); Bartunek et al., Cytokine 8(1):14-20 (1996) (which are all incorporated by reference herein in their entireties).

Antibodies of the present invention may be used, for example, but not limited to, to purify, detect, and target the polypeptides of the present invention, including both in vitro and in vivo diagnostic and therapeutic methods. For example, the antibodies have use in immunoassays for qualitatively and quantitatively measuring levels of the polypeptides of the present invention in biological samples. See, e.g., Harlow et al., Antibodies: A Laboratory Manual, (Cold Spring Harbor Laboratory Press, 2nd ed. 1988) (incorporated by reference herein in its entirety).

As discussed in more detail below, the antibodies of the present invention may be used either alone or in combination with other compositions. The antibodies may further be recombinantly fused to a heterologous polypeptide at the N- or C-terminus or chemically conjugated (including covalently and non-covalently conjugations) to polypeptides or other compositions. For example, antibodies of the present invention may be recombinantly fused or conjugated to molecules useful as labels in detection assays and effector molecules such as heterologous polypeptides, drugs, radionuclides, or toxins. See, e.g., PCT publications WO 92/08495; WO 91/14438; WO 89/12624; U.S. Patent No. 5,314,995; and EP 396,387.

The antibodies of the invention include derivatives that are modified, i.e, by the covalent attachment of any type of molecule to the antibody such that covalent attachment does not prevent the antibody from generating an anti-idiotypic response. For example, but not by way of limitation, the antibody derivatives include antibodies that have been modified, e.g., by glycosylation, acetylation, pegylation, phosphylation, amidation, derivatization by known protecting/blocking groups, proteolytic cleavage, linkage to a cellular ligand or other protein, etc. Any of

numerous chemical modifications may be carried out by known techniques, including, but not limited to specific chemical cleavage, acetylation, formylation, metabolic synthesis of tunicamycin, etc. Additionally, the derivative may contain one or more non-classical amino acids.

The antibodies of the present invention may be generated by any suitable method known in the art. Polyclonal antibodies to an antigen-of- interest can be produced by various procedures well known in the art. For example, a polypeptide of the invention can be administered to various host animals including, but not limited to, rabbits, mice, rats, etc. to induce the production of sera containing polyclonal antibodies specific for the antigen. Various adjuvants may be used to increase the immunological response, depending on the host species, and include but are not limited to, Freund's (complete and incomplete), mineral gels such as aluminum hydroxide, surface active substances such as lysolecithin, pluronic polyols, polyanions, peptides, oil emulsions, keyhole limpet hemocyanins, dinitrophenol, and potentially useful human adjuvants such as BCG (bacille Calmette-Guerin) and corynebacterium parvum. Such adjuvants are also well known in the art.

Monoclonal antibodies can be prepared using a wide variety of techniques known in the art including the use of hybridoma, recombinant, and phage display technologies, or a combination thereof. For example, monoclonal antibodies can be produced using hybridoma techniques including those known in the art and taught, for example, in Harlow et al., Antibodies: A Laboratory Manual, (Cold Spring Harbor Laboratory Press, 2nd ed. 1988); Hammerling, et al., in: Monoclonal Antibodies and T-Cell Hybridomas 563-681 (Elsevier, N.Y., 1981) (said references incorporated by reference in their entireties). The term "monoclonal antibody" as used herein is not limited to antibodies produced through hybridoma technology. The term "monoclonal antibody" refers to an antibody that is derived from a single clone, including any eukaryotic, prokaryotic, or phage clone, and not the method by which it is produced.

Methods for producing and screening for specific antibodies using hybridoma technology are routine and well known in the art and are discussed in detail in the Examples (e.g., Example 16). In a non-limiting example, mice can be immunized with a polypeptide of the invention or a cell expressing such peptide. Once an

immune response is detected, e.g., antibodies specific for the antigen are detected in the mouse serum, the mouse spleen is harvested and splenocytes isolated. The splenocytes are then fused by well known techniques to any suitable myeloma cells, for example cells from cell line SP20 available from the ATCC. Hybridomas are selected and cloned by limited dilution. The hybridoma clones are then assayed by methods known in the art for cells that secrete antibodies capable of binding a polypeptide of the invention. Ascites fluid, which generally contains high levels of antibodies, can be generated by immunizing mice with positive hybridoma clones.

Accordingly, the present invention provides methods of generating monoclonal antibodies as well as antibodies produced by the method comprising culturing a hybridoma cell secreting an antibody of the invention wherein, preferably, the hybridoma is generated by fusing splenocytes isolated from a mouse immunized with an antigen of the invention with myeloma cells and then screening the hybridomas resulting from the fusion for hybridoma clones that secrete an antibody able to bind a polypeptide of the invention.

Antibody fragments which recognize specific epitopes may be generated by known techniques. For example, Fab and F(ab')2 fragments of the invention may be produced by proteolytic cleavage of immunoglobulin molecules, using enzymes such as papain (to produce Fab fragments) or pepsin (to produce F(ab')2 fragments). F(ab')2 fragments contain the variable region, the light chain constant region and the CH1 domain of the heavy chain.

For example, the antibodies of the present invention can also be generated using various phage display methods known in the art. In phage display methods, functional antibody domains are displayed on the surface of phage particles which carry the polynucleotide sequences encoding them. In a particular embodiment, such phage can be utilized to display antigen binding domains expressed from a repertoire or combinatorial antibody library (e.g., human or murine). Phage expressing an antigen binding domain that binds the antigen of interest can be selected or identified with antigen, e.g., using labeled antigen or antigen bound or captured to a solid surface or bead. Phage used in these methods are typically filamentous phage including fd and M13 binding domains expressed from phage with Fab, Fv or disulfide stabilized Fv antibody domains recombinantly fused to either the phage

gene III or gene VIII protein. Examples of phage display methods that can be used to make the antibodies of the present invention include those disclosed in Brinkman et al., J. Immunol. Methods 182:41-50 (1995); Ames et al., J. Immunol. Methods 184:177-186 (1995); Kettleborough et al., Eur. J. Immunol. 24:952-958 (1994); Persic et al., Gene 187 9-18 (1997); Burton et al., Advances in Immunology 57:191-280 (1994); PCT application No. PCT/GB91/01134; PCT publications WO 90/02809; WO 91/10737; WO 92/01047; WO 92/18619; WO 93/11236; WO 95/15982; WO 95/20401; and U.S. Patent Nos. 5,698,426; 5,223,409; 5,403,484; 5,580,717; 5,427,908; 5,750,753; 5,821,047; 5,571,698; 5,427,908; 5,516,637; 5,780,225; 5,658,727; 5,733,743 and 5,969,108; each of which is incorporated herein by reference in its entirety.

As described in the above references, after phage selection, the antibody coding regions from the phage can be isolated and used to generate whole antibodies, including human antibodies, or any other desired antigen binding fragment, and expressed in any desired host, including mammalian cells, insect cells, plant cells, yeast, and bacteria, e.g., as described in detail below. For example, techniques to recombinantly produce Fab, Fab' and F(ab')2 fragments can also be employed using methods known in the art such as those disclosed in PCT publication WO 92/22324; Mullinax et al., BioTechniques 12(6):864-869 (1992); and Sawai et al., AJRI 34:26-34 (1995); and Better et al., Science 240:1041-1043 (1988) (said references incorporated by reference in their entireties).

Examples of techniques which can be used to produce single-chain Fvs and antibodies include those described in U.S. Patents 4,946,778 and 5,258,498; Huston et al., Methods in Enzymology 203:46-88 (1991); Shu et al., PNAS 90:7995-7999 (1993); and Skerra et al., Science 240:1038-1040 (1988). For some uses, including in vivo use of antibodies in humans and in vitro detection assays, it may be preferable to use chimeric, humanized, or human antibodies. A chimeric antibody is a molecule in which different portions of the antibody are derived from different animal species, such as antibodies having a variable region derived from a murine monoclonal antibody and a human immunoglobulin constant region. Methods for producing chimeric antibodies are known in the art. See e.g., Morrison, Science 229:1202 (1985); Oi et al., BioTechniques 4:214 (1986); Gillies et al., (1989) J. Immunol.

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Methods 125:191-202; U.S. Patent Nos. 5,807,715; 4,816,567; and 4,816397, which are incorporated herein by reference in their entirety. Humanized antibodies are antibody molecules from non-human species antibody that binds the desired antigen having one or more complementarity determining regions (CDRs) from the non-human species and a framework regions from a human immunoglobulin molecule. Often, framework residues in the human framework regions will be substituted with the corresponding residue from the CDR donor antibody to alter, preferably improve, antigen binding. These framework substitutions are identified by methods well known in the art, e.g., by modeling of the interactions of the CDR and framework residues to identify framework residues important for antigen binding and sequence comparison to identify unusual framework residues at particular positions. (See, e.g., Queen et al., U.S. Patent No. 5,585,089; Riechmann et al., Nature 332:323 (1988), which are incorporated herein by reference in their entireties.) Antibodies can be humanized using a variety of techniques known in the art including, for example, CDR-grafting (EP 239,400; PCT publication WO 91/09967; U.S. Patent Nos. 5,225,539; 5,530,101; and 5,585,089), veneering or resurfacing (EP 592,106; EP 519,596; Padlan, Molecular Immunology 28(4/5):489-498 (1991); Studnicka et al., Protein Engineering 7(6):805-814 (1994); Roguska. et al., PNAS 91:969-973 (1994)), and chain shuffling (U.S. Patent No. 5,565,332).

Completely human antibodies are particularly desirable for therapeutic treatment of human patients. Human antibodies can be made by a variety of methods known in the art including phage display methods described above using antibody libraries derived from human immunoglobulin sequences. See also, U.S. Patent Nos. 4,444,887 and 4,716,111; and PCT publications WO 98/46645, WO 98/50433, WO 98/24893, WO 98/16654, WO 96/34096, WO 96/33735, and WO 91/10741; each of which is incorporated herein by reference in its entirety.

Human antibodies can also be produced using transgenic mice which are incapable of expressing functional endogenous immunoglobulins, but which can express human immunoglobulin genes. For example, the human heavy and light chain immunoglobulin gene complexes may be introduced randomly or by homologous recombination into mouse embryonic stem cells. Alternatively, the human variable region, constant region, and diversity region may be introduced into

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mouse embryonic stem cells in addition to the human heavy and light chain genes. The mouse heavy and light chain immunoglobulin genes may be rendered non-functional separately or simultaneously with the introduction of human immunoglobulin loci by homologous recombination. In particular, homozygous deletion of the JH region prevents endogenous antibody production. The modified embryonic stem cells are expanded and microinjected into blastocysts to produce chimeric mice. The chimeric mice are then bred to produce homozygous offspring which express human antibodies. The transgenic mice are immunized in the normal fashion with a selected antigen, e.g., all or a portion of a polypeptide of the invention. Monoclonal antibodies directed against the antigen can be obtained from the immunized, transgenic mice using conventional hybridoma technology. The human immunoglobulin transgenes harbored by the transgenic mice rearrange during B cell differentiation, and subsequently undergo class switching and somatic mutation. Thus, using such a technique, it is possible to produce therapeutically useful IgG, IgA, IgM and IgE antibodies. For an overview of this technology for producing human antibodies, see Lonberg and Huszar, Int. Rev. Immunol. 13:65-93 (1995). For a detailed discussion of this technology for producing human antibodies and human monoclonal antibodies and protocols for producing such antibodies, see, e.g., PCT publications WO 98/24893; WO 92/01047; WO 96/34096; WO 96/33735; European Patent No. 0 598 877; U.S. Patent Nos. 5,413,923; 5,625,126; 5,633,425; 5,569,825; 5,661,016; 5,545,806; 5,814,318; 5,885,793; 5,916,771; and 5,939,598, which are incorporated by reference herein in their entirety. In addition, companies such as Abgenix, Inc. (Freemont, CA) and Genpharm (San Jose, CA) can be engaged to provide human antibodies directed against a selected antigen using technology similar to that described above.

Completely human antibodies which recognize a selected epitope can be generated using a technique referred to as "guided selection." In this approach a selected non-human monoclonal antibody, e.g., a mouse antibody, is used to guide the selection of a completely human antibody recognizing the same epitope. (Jespers et al., Bio/technology 12:899-903 (1988)).

Further, antibodies to the polypeptides of the invention can, in turn, be utilized to generate anti-idiotype antibodies that "mimic" polypeptides of the invention using

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techniques well known to those skilled in the art. (See, e.g., Greenspan & Bona, FASEB J. 7(5):437-444; (1989) and Nissinoff, J. Immunol. 147(8):2429-2438 (1991)). For example, antibodies which bind to and competitively inhibit polypeptide multimerization and/or binding of a polypeptide of the invention to a ligand can be used to generate anti-idiotypes that "mimic" the polypeptide multimerization and/or binding domain and, as a consequence, bind to and neutralize polypeptide and/or its ligand. Such neutralizing anti-idiotypes or Fab fragments of such anti-idiotypes can be used in therapeutic regimens to neutralize polypeptide ligand. For example, such anti-idiotypic antibodies can be used to bind a polypeptide of the invention and/or to bind its ligands/receptors, and thereby block its biological activity.

Polynucleotides Encoding Antibodies

The invention further provides polynucleotides comprising a nucleotide sequence encoding an antibody of the invention and fragments thereof. The invention also encompasses polynucleotides that hybridize under stringent or lower stringency hybridization conditions, e.g., as defined supra, to polynucleotides that encode an antibody, preferably, that specifically binds to a polypeptide of the invention, preferably, an antibody that binds to a polypeptide having the amino acid sequence of SEQ ID NO:Y.

The polynucleotides may be obtained, and the nucleotide sequence of the polynucleotides determined, by any method known in the art. For example, if the nucleotide sequence of the antibody is known, a polynucleotide encoding the antibody may be assembled from chemically synthesized oligonucleotides (e.g., as described in Kutmeier et al., BioTechniques 17:242 (1994)), which, briefly, involves the synthesis of overlapping oligonucleotides containing portions of the sequence encoding the antibody, annealing and ligating of those oligonucleotides, and then amplification of the ligated oligonucleotides by PCR.

Alternatively, a polynucleotide encoding an antibody may be generated from nucleic acid from a suitable source. If a clone containing a nucleic acid encoding a particular antibody is not available, but the sequence of the antibody molecule is known, a nucleic acid encoding the immunoglobulin may be chemically synthesized or obtained from a suitable source (e.g., an antibody cDNA library, or a cDNA library

generated from, or nucleic acid, preferably poly A+ RNA, isolated from, any tissue or cells expressing the antibody, such as hybridoma cells selected to express an antibody of the invention) by PCR amplification using synthetic primers hybridizable to the 3' and 5' ends of the sequence or by cloning using an oligonucleotide probe specific for the particular gene sequence to identify, e.g., a cDNA clone from a cDNA library that encodes the antibody. Amplified nucleic acids generated by PCR may then be cloned into replicable cloning vectors using any method well known in the art.

Once the nucleotide sequence and corresponding amino acid sequence of the antibody is determined, the nucleotide sequence of the antibody may be manipulated using methods well known in the art for the manipulation of nucleotide sequences, e.g., recombinant DNA techniques, site directed mutagenesis, PCR, etc. (see, for example, the techniques described in Sambrook et al., 1990, Molecular Cloning, A Laboratory Manual, 2d Ed., Cold Spring Harbor Laboratory, Cold Spring Harbor, NY and Ausubel et al., eds., 1998, Current Protocols in Molecular Biology, John Wiley & Sons, NY, which are both incorporated by reference herein in their entireties), to generate antibodies having a different amino acid sequence, for example to create amino acid substitutions, deletions, and/or insertions.

In a specific embodiment, the amino acid sequence of the heavy and/or light chain variable domains may be inspected to identify the sequences of the complementarity determining regions (CDRs) by methods that are well know in the art, e.g., by comparison to known amino acid sequences of other heavy and light chain variable regions to determine the regions of sequence hypervariability. Using routine recombinant DNA techniques, one or more of the CDRs may be inserted within framework regions, e.g., into human framework regions to humanize a non-human antibody, as described supra. The framework regions may be naturally occurring or consensus framework regions, and preferably human framework regions (see, e.g., Chothia et al., J. Mol. Biol. 278: 457-479 (1998) for a listing of human framework regions). Preferably, the polynucleotide generated by the combination of the framework regions and CDRs encodes an antibody that specifically binds a polypeptide of the invention. Preferably, as discussed supra, one or more amino acid substitutions may be made within the framework regions, and, preferably, the amino

acid substitutions improve binding of the antibody to its antigen. Additionally, such methods may be used to make amino acid substitutions or deletions of one or more variable region cysteine residues participating in an intrachain disulfide bond to generate antibody molecules lacking one or more intrachain disulfide bonds. Other alterations to the polynucleotide are encompassed by the present invention and within the skill of the art.

In addition, techniques developed for the production of "chimeric antibodies" (Morrison et al., Proc. Natl. Acad. Sci. 81:851-855 (1984); Neuberger et al., Nature 312:604-608 (1984); Takeda et al., Nature 314:452-454 (1985)) by splicing genes from a mouse antibody molecule of appropriate antigen specificity together with genes from a human antibody molecule of appropriate biological activity can be used. As described supra, a chimeric antibody is a molecule in which different portions are derived from different animal species, such as those having a variable region derived from a murine mAb and a human immunoglobulin constant region, e.g., humanized antibodies.

Alternatively, techniques described for the production of single chain antibodies (U.S. Patent No. 4,946,778; Bird, Science 242:423- 42 (1988); Huston et al., Proc. Natl. Acad. Sci. USA 85:5879-5883 (1988); and Ward et al., Nature 334:544-54 (1989)) can be adapted to produce single chain antibodies. Single chain antibodies are formed by linking the heavy and light chain fragments of the Fv region via an amino acid bridge, resulting in a single chain polypeptide. Techniques for the assembly of functional Fv fragments in E. coli may also be used (Skerra et al., Science 242:1038- 1041 (1988)).

Methods of Producing Antibodies

The antibodies of the invention can be produced by any method known in the art for the synthesis of antibodies, in particular, by chemical synthesis or preferably, by recombinant expression techniques.

Recombinant expression of an antibody of the invention, or fragment, derivative or analog thereof, (e.g., a heavy or light chain of an antibody of the invention or a single chain antibody of the invention), requires construction of an expression vector containing a polynucleotide that encodes the antibody. Once a

polynucleotide encoding an antibody molecule or a heavy or light chain of an antibody, or portion thereof (preferably containing the heavy or light chain variable domain), of the invention has been obtained, the vector for the production of the antibody molecule may be produced by recombinant DNA technology using techniques well known in the art. Thus, methods for preparing a protein by expressing a polynucleotide containing an antibody encoding nucleotide sequence are described herein. Methods which are well known to those skilled in the art can be used to construct expression vectors containing antibody coding sequences and appropriate transcriptional and translational control signals. These methods include, for example, in vitro recombinant DNA techniques, synthetic techniques, and in vivo genetic recombination. The invention, thus, provides replicable vectors comprising a nucleotide sequence encoding an antibody molecule of the invention, or a heavy or light chain thereof, or a heavy or light chain variable domain, operably linked to a promoter. Such vectors may include the nucleotide sequence encoding the constant region of the antibody molecule (see, e.g., PCT Publication WO 86/05807; PCT Publication WO 89/01036; and U.S. Patent No. 5,122,464) and the variable domain of the antibody may be cloned into such a vector for expression of the entire heavy or light chain.

The expression vector is transferred to a host cell by conventional techniques and the transfected cells are then cultured by conventional techniques to produce an antibody of the invention. Thus, the invention includes host cells containing a polynucleotide encoding an antibody of the invention, or a heavy or light chain thereof, or a single chain antibody of the invention, operably linked to a heterologous promoter. In preferred embodiments for the expression of double-chained antibodies, vectors encoding both the heavy and light chains may be co-expressed in the host cell for expression of the entire immunoglobulin molecule, as detailed below.

A variety of host-expression vector systems may be utilized to express the antibody molecules of the invention. Such host-expression systems represent vehicles by which the coding sequences of interest may be produced and subsequently purified, but also represent cells which may, when transformed or transfected with the appropriate nucleotide coding sequences, express an antibody molecule of the invention in situ. These include but are not limited to microorganisms such as

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bacteria (e.g., E. coli, B. subtilis) transformed with recombinant bacteriophage DNA, plasmid DNA or cosmid DNA expression vectors containing antibody coding sequences; yeast (e.g., Saccharomyces, Pichia) transformed with recombinant yeast expression vectors containing antibody coding sequences; insect cell systems infected with recombinant virus expression vectors (e.g., baculovirus) containing antibody coding sequences; plant cell systems infected with recombinant virus expression vectors (e.g., cauliflower mosaic virus, CaMV; tobacco mosaic virus, TMV) or transformed with recombinant plasmid expression vectors (e.g., Ti plasmid) containing antibody coding sequences; or mammalian cell systems (e.g., COS, CHO, BHK, 293, 3T3 cells) harboring recombinant expression constructs containing promoters derived from the genome of mammalian cells (e.g., metallothionein promoter) or from mammalian viruses (e.g., the adenovirus late promoter; the vaccinia virus 7.5K promoter). Preferably, bacterial cells such as Escherichia coli, and more preferably, eukaryotic cells, especially for the expression of whole recombinant antibody molecule, are used for the expression of a recombinant antibody molecule. For example, mammalian cells such as Chinese hamster ovary cells (CHO), in conjunction with a vector such as the major intermediate early gene promoter element from human cytomegalovirus is an effective expression system for antibodies (Foecking et al., Gene 45:101 (1986); Cockett et al., Bio/Technology 8:2 (1990)).

In bacterial systems, a number of expression vectors may be advantageously selected depending upon the use intended for the antibody molecule being expressed. For example, when a large quantity of such a protein is to be produced, for the generation of pharmaceutical compositions of an antibody molecule, vectors which direct the expression of high levels of fusion protein products that are readily purified may be desirable. Such vectors include, but are not limited, to the E. coli expression vector pUR278 (Ruther et al., EMBO J. 2:1791 (1983)), in which the antibody coding sequence may be ligated individually into the vector in frame with the lac Z coding region so that a fusion protein is produced; pIN vectors (Inouye & Inouye, Nucleic Acids Res. 13:3101-3109 (1985); Van Heeke & Schuster, J. Biol. Chem. 24:5503-5509 (1989)); and the like. pGEX vectors may also be used to express foreign polypeptides as fusion proteins with glutathione S-transferase (GST). In general, such

fusion proteins are soluble and can easily be purified from lysed cells by adsorption and binding to matrix glutathione-agarose beads followed by elution in the presence of free glutathione. The pGEX vectors are designed to include thrombin or factor Xa protease cleavage sites so that the cloned target gene product can be released from the GST moiety.

In an insect system, Autographa californica nuclear polyhedrosis virus (AcNPV) is used as a vector to express foreign genes. The virus grows in *Spodoptera frugiperda* cells. The antibody coding sequence may be cloned individually into non-essential regions (for example the polyhedrin gene) of the virus and placed under control of an AcNPV promoter (for example the polyhedrin promoter).

In mammalian host cells, a number of viral-based expression systems may be utilized. In cases where an adenovirus is used as an expression vector, the antibody coding sequence of interest may be ligated to an adenovirus transcription/translation control complex, e.g., the late promoter and tripartite leader sequence. This chimeric gene may then be inserted in the adenovirus genome by in vitro or in vivo recombination. Insertion in a non- essential region of the viral genome (e.g., region E1 or E3) will result in a recombinant virus that is viable and capable of expressing the antibody molecule in infected hosts. (e.g., see Logan & Shenk, Proc. Natl. Acad. Sci. USA 81:355-359 (1984)). Specific initiation signals may also be required for efficient translation of inserted antibody coding sequences. These signals include the ATG initiation codon and adjacent sequences. Furthermore, the initiation codon must be in phase with the reading frame of the desired coding sequence to ensure translation of the entire insert. These exogenous translational control signals and initiation codons can be of a variety of origins, both natural and synthetic. The efficiency of expression may be enhanced by the inclusion of appropriate transcription enhancer elements, transcription terminators, etc. (see Bittner et al., Methods in Enzymol. 153:51-544 (1987)).

In addition, a host cell strain may be chosen which modulates the expression of the inserted sequences, or modifies and processes the gene product in the specific fashion desired. Such modifications (e.g., glycosylation) and processing (e.g., cleavage) of protein products may be important for the function of the protein.

Different host cells have characteristic and specific mechanisms for the post-translational processing and modification of proteins and gene products. Appropriate cell lines or host systems can be chosen to ensure the correct modification and processing of the foreign protein expressed. To this end, eukaryotic host cells which possess the cellular machinery for proper processing of the primary transcript, glycosylation, and phosphorylation of the gene product may be used. Such mammalian host cells include but are not limited to CHO, VERY, BHK, Hela, COS, MDCK, 293, 3T3, WI38, and in particular, breast cancer cell lines such as, for example, BT483, Hs578T, HTB2, BT20 and T47D, and normal mammary gland cell line such as, for example, CRL7030 and Hs578Bst.

For long-term, high-yield production of recombinant proteins, stable expression is preferred. For example, cell lines which stably express the antibody molecule may be engineered. Rather than using expression vectors which contain viral origins of replication, host cells can be transformed with DNA controlled by appropriate expression control elements (e.g., promoter, enhancer, sequences, transcription terminators, polyadenylation sites, etc.), and a selectable marker. Following the introduction of the foreign DNA, engineered cells may be allowed to grow for 1-2 days in an enriched media, and then are switched to a selective media. The selectable marker in the recombinant plasmid confers resistance to the selection and allows cells to stably integrate the plasmid into their chromosomes and grow to form foci which in turn can be cloned and expanded into cell lines. This method may advantageously be used to engineer cell lines which express the antibody molecule. Such engineered cell lines may be particularly useful in screening and evaluation of compounds that interact directly or indirectly with the antibody molecule.

A number of selection systems may be used, including but not limited to the herpes simplex virus thymidine kinase (Wigler et al., Cell 11:223 (1977)), hypoxanthine-guanine phosphoribosyltransferase (Szybalska & Szybalski, Proc. Natl. Acad. Sci. USA 48:202 (1992)), and adenine phosphoribosyltransferase (Lowy et al., Cell 22:817 (1980)) genes can be employed in tk-, hgprt- or aprt- cells, respectively. Also, antimetabolite resistance can be used as the basis of selection for the following genes: dhfr, which confers resistance to methotrexate (Wigler et al., Natl. Acad. Sci. USA 77:357 (1980); O'Hare et al., Proc. Natl. Acad. Sci. USA 78:1527 (1981)); gpt,